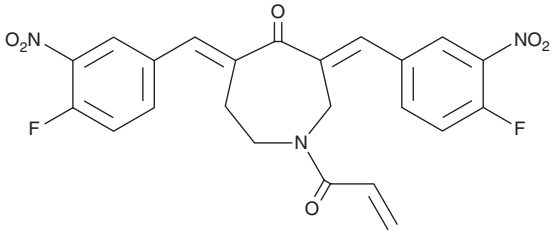
PRODUCT INFORMATION

VLX1570

Item No. 29721

CAS Registry No.:	1431280-51-1
Formal Name:	3,5-*bis*[(4-fluoro-3-nitrophenyl) methylene]hexahydro-1-(1-oxo-2-propen-1-yl)-4H-azepin-4-one
MF:	$C_{23}H_{17}F_2N_3O_6$
FW:	469.4
Purity:	≥98%
UV/Vis.:	λ_{max}: 296 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

VLX1570 is supplied as a crystalline solid. A stock solution may be made by dissolving the VLX1570 in the solvent of choice, which should be purged with an inert gas. VLX1570 is soluble in organic solvents such as DMSO and dimethyl formamide (DMF). The solubility of VLX1570 in these solvents is approximately 16 and 25 mg/ml, respectively. VLX1570 is also slightly soluble in ethanol.

VLX1570 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, VLX1570 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. VLX1570 has a solubility of approximately 0.3 mg/ml in a 1:2 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

VLX1570 is an inhibitor of 19S proteasomal deubiquitinases with IC_{50} values of 6.4 and 13 µM for deubiquitinase activity *in vitro* using Ub-rhodamine and Ub-AMC, respectively, as substrates.[1,2] It is selective for proteasomal deubiquitinases over a panel of deubiquitinases at 20 µM, but inhibits USP5 by greater than 50%, and over a panel of 211 kinases at 10 µM, but inhibits Cdk4 by 77%.[1] VLX1570 binds to and inhibits recombinant ubiquitin-specific protease 14 (USP14) and ubiquitin carboxyl-terminal hydrolase isozyme L5 (UCHL5) *in vitro*, and inhibits the USP14 and UCHL5 activity of purified 19S proteasomes when used at a concentration of 50 µM.[1,2] It inhibits the proliferation of KMS-11, RPMI-8226, OPM-2, and OPM-2-BZ^R multiple myeloma cells (IC_{50}s = 43, 74, 126, and 191 nM, respectively), as well as induces apoptosis and increases the accumulation of polyubiquitinated proteins.[2] VLX1570 (3 mg/kg per day for 10 days) increases survival and reduces tumor growth in KMS-11-LUC2 and RPMI-8226 mouse xenograft models, respectively.

References

1. Wang, X., D'Arcy, P., Caulfield, T.R., *et al.* Synthesis and evaluation of derivatives of the proteasome deubiquitinase inhibitor b-AP15. *Chem. Biol. Drug Des.* **86(5)**, 1036-1048 (2015).
2. Wang, X., Mazurkiewicz, M., Hillert, E.-K., *et al.* The proteasome deubiquitinase inhibitor VLX1570 shows selectivity for ubiquitin-specific protease-14 and induces apoptosis of multiple myeloma cells. *Sci. Rep.* **6:26979** (2016).

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