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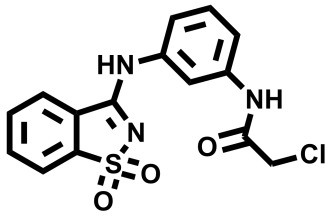
ATPase VCP/p97 Inhibitor – NMS-859

Chemical Name: 2-chloro-N-(3-((1,1-dioxidobenzo[d]isothiazol-3-yl)amino)phenyl)acetamide



Molecular Weight:	349.79
Formula:	$C_{15}H_{12}ClN_3O_3S$
Purity:	≥98%
CAS#:	1449236-96-7
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

NMS-859 is a potent and specific small molecule covalent inhibitor of the ATPase VCP/p97 (IC_{50} ~0.37 μM), identified by high-throughput screening. It is very selective (IC_{50} >10 μM) against all of the AAA ATPases, HSP90 or the 53 kinases tested. NMS-859 was active in a cell proliferation assay, with IC_{50} values of 3.5 μM and 3.0 μM in HCT116 and HeLa cell lines, respectively. NMS-859 covalently modifies VCP on the active site Cys522 and blocks ATP binding. NMS-859 provided critical validation of VCP as a cancer target, and it raises the possibility that targeting VCP might prevent proteasome inhibitor–resistant tumors from escaping through the aggresome-autophagy pathways and cause them to collapse under the high load of unfolded proteins.

How to Use:

In vitro: NMS-859 was used at 2.5-10 μM final concentration in various in vitro assays.

In vivo: n/a

Reference:

1. Magnaghi P, et al. Covalent and allosteric inhibitors of the ATPase VCP/p97 induce cancer cell death. (2013) Nat Chem Biol. 9(9):548-56

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