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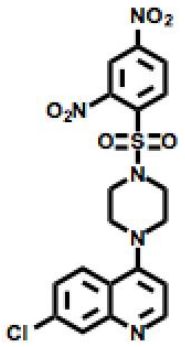
Proteasome Inhibitor – VR23

Chemical Name: 7-chloro-4-(4-((2,4-dinitrophenyl)sulfonyl)piperazin-1-yl)quinoline



Molecular Weight:	477.88
Formula:	$C_{19}H_{16}ClN_5O_6S$
Purity:	≥98%
CAS#:	1624602-30-7
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

VR23 is a potent and selective proteasome inhibitor with IC_{50} of 1 nM, 50-100 nM, and 3 μM for trypsin-like proteasomes, chymotrypsin-like proteasomes, and caspase-like proteasomes, respectively. Data from molecular docking and substrate competition assays established that the primary molecular target of VR23 was β2 of the 20S proteasome catalytic subunit. VR23 was structurally distinct from other known proteasome inhibitors and selectively killed cancer cells by apoptosis, with little effect on noncancerous cells. Mechanistic investigations showed that cancer cells exposed to VR23 underwent an abnormal centrosome amplification cycle caused by the accumulation of ubiquitinated cyclin E. In combinations with the clinically approved chymotrypsin-like proteasome inhibitor bortezomib, VR23 produced a synergistic effect in killing multiple myeloma cells, including those that were resistant to bortezomib. VR23 was effective in vivo in controlling multiple myelomas and metastatic breast cancer cells, in the latter case also enhancing the antitumor activity of paclitaxel while reducing its side effects.

How to Use:

In vitro: VR23 was used at 10-20 μM final concentration in various assays.

In vivo: VR23 was dosed to ATH490 athymic mice engrafted with MDA-MB-231 or RPMI 8226 cancer cells at 30 mg/Kg by IP injection once per day.

Reference:

1. Pundir S, et al. VR23: A Quinoline-Sulfonyl Hybrid Proteasome Inhibitor That Selectively Kills Cancer via Cyclin E-Mediated Centrosome Amplification. (2015) Cancer Res. 75(19):4164-75.