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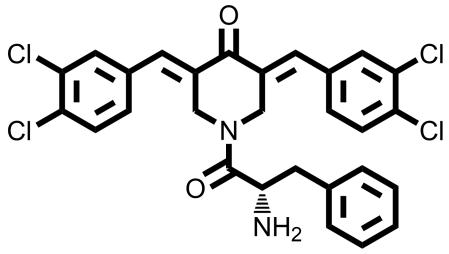
Ubiquitin Receptor RPN13/ADRM1 Inhibitor – RA190

Chemical Name: (3E,5E)-1-((S)-2-amino-3-phenylpropanoyl)-3,5-bis(3,4-dichlorobenzylidene)piperidin-4-one



Molecular Weight:	560.30
Formula:	$C_{28}H_{22}Cl_4N_2O_2$
Purity:	≥98%
CAS#:	1617495-03-0
Solubility:	DMSO up to 50 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

RA190 is a novel potent and selective inhibitor of proteasome Ubiquitin receptor RPN13/ADRM1. It covalently binds to the cysteine 88 of ubiquitin receptor RPN13 in the 19S regulatory particle and inhibits proteasome function, triggering rapid accumulation of polyubiquitinated proteins. Multiple myeloma (MM) lines, even those resistant to bortezomib, were sensitive to RA190 via endoplasmic reticulum stress-related apoptosis. RA190 stabilized targets of human papillomavirus (HPV) E6 oncoprotein, and preferentially killed HPV-transformed cells. After oral or intraperitoneal dosing in mice, RA190 distributed to plasma and major organs except the brain, and inhibited proteasome function in skin and muscle. RA190 administration profoundly reduced growth of MM and ovarian cancer xenografts, and oral RA190 treatment retarded HPV16(+) syngeneic mouse tumor growth, without affecting spontaneous HPV-specific CD8(+) T cell responses, suggesting its therapeutic potential.

How to Use:

In vitro: RA190 was used at 1-10 μM final concentration in various in vitro assays.

In vivo: RA190 was administered by intraperitoneal injection once a day at a dose of 20 mg/kg in tumor models.

Reference:

1. Anchoori RK, et al. A bis-Benzylidine Piperidone Targeting Proteasome Ubiquitin Receptor RPN13/ADRM1 as a Therapy for Cancer. (2013) Cancer Cell. 24(6):791-805.