

LDN193189

Catalog No: tcsc0669



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg



Specifications

CAS No:

1062368-24-4

Formula:

$C_{25}H_{22}N_6$

Pathway:

TGF-beta/Smad

Target:

TGF- β Receptor

Purity / Grade:

>98%

Solubility:

H₂O :

Alternative Names:

DM-3189

Observed Molecular Weight:

406.48

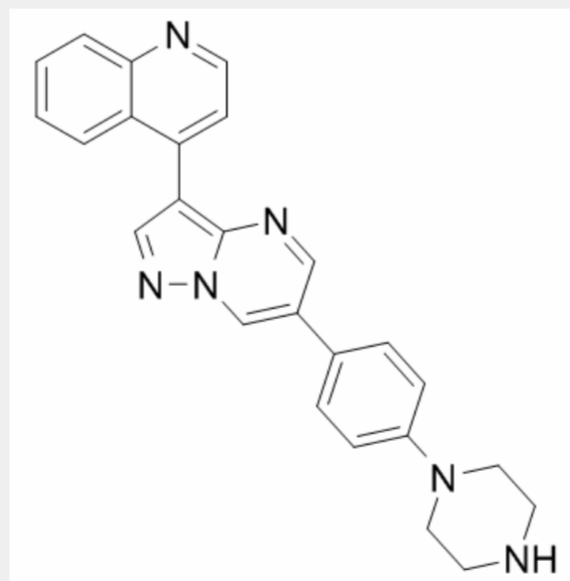
Product Description

LDN193189 is a selective **BMP** type I receptor kinases inhibitor, which inhibits transcriptional activity of the BMP type I receptors **ALK2** and **ALK3** (IC_{50} =5 nM and 30 nM, respectively), with substantially weaker effects on activin and the TGF- β type I receptors ALK4, ALK5 and ALK7 (IC_{50} \geq 500 nM).

IC50 & Target: IC50: 5 nM (ALK2), 30 nM (ALK3)^[1]

In Vitro: LDN-193189 inhibits BMP4-mediated Smad1, Smad5 and Smad8 activation with greater potency than did dorsomorphin (IC_{50} =5 nM versus 470 nM) while retaining 200-fold selectivity for BMP signaling versus TGF- β signaling (IC_{50} for TGF- β \geq 1,000 nM). LDN-193189 efficiently inhibits transcriptional activity of the BMP type I receptors ALK2 and ALK3 (IC_{50} =5 nM and 30 nM, respectively), with substantially weaker effects on activin and the TGF- β type I receptors ALK4, ALK5 and ALK7 (IC_{50} \geq 500 nM) and increases selectivity for BMP signaling versus AMP-activated protein kinase, PDGFR and MAPK signaling pathways as compared to the parent compound. LDN-193189 blocks the transcriptional activity induced by either constitutively active ALK2^{R206H} or ALK2^{Q207D} mutant proteins. These findings suggest that LDN-193189 might affect BMP-induced osteoblast differentiation. In fact, LDN-193189 inhibits the induction of alkaline phosphatase activity in C2C12 cells by BMP4 even when administered 12 h after BMP stimulation, indicating sustained BMP signaling activity is needed for osteogenic differentiation^[1].

In Vivo: In the first experiment, LDN-193189 (3 mg/kg) is injected intraperitoneally twice a day after tumors became palpable 7 days post-implantation. The growth rates between the control vehicle- and LDN-193189-treated mice are not significantly different after the first 5 weeks, but differences in the growth rates are detected after 6 and 7 weeks post-treatment. In the second experiment, cells are isolated from PCa-118b tumors and injected subcutaneously into SCID mice (1×10^6 cells per mouse). LDN-193189 or vehicle is applied to mice 5 days post-tumor cell injection before tumors are palpable. The differences in the average growth rates between these two groups, as measured by tumor size, are significant at 6 and 7 weeks post-treatment. The tumor weights also show significant differences at the termination of the study at week 7. The X-ray of the tumors shows that the ectopic bone volume and bone density are reduced in the tumors of LDN-193189-treated group compared to that of controls^[2]. Co-incubation of pulmonary arterial smooth muscle cells (PASMCs) from the pulmonary arterial hypertension (PAH) rats with Sildenafil and LDN-193189 completely inhibited the anti-proliferation and up-regulation of the bone morphogenetic protein (BMPR2) and Cx40 expression by the Sildenafil^[3].



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