

# LDN193189 (Hydrochloride)

Catalog No: tcsc0670



## Available Sizes

**Size:** 5mg

**Size:** 10mg

**Size:** 50mg



## Specifications

**CAS No:**

1062368-62-0

**Formula:**

$C_{25}H_{26}Cl_4N_6$

**Pathway:**

TGF-beta/Smad

**Target:**

TGF- $\beta$  Receptor

**Purity / Grade:**

>98%

**Solubility:**

H<sub>2</sub>O : 20 mg/mL (36.21 mM; Need ultrasonic and warming)

**Observed Molecular Weight:**

552.33

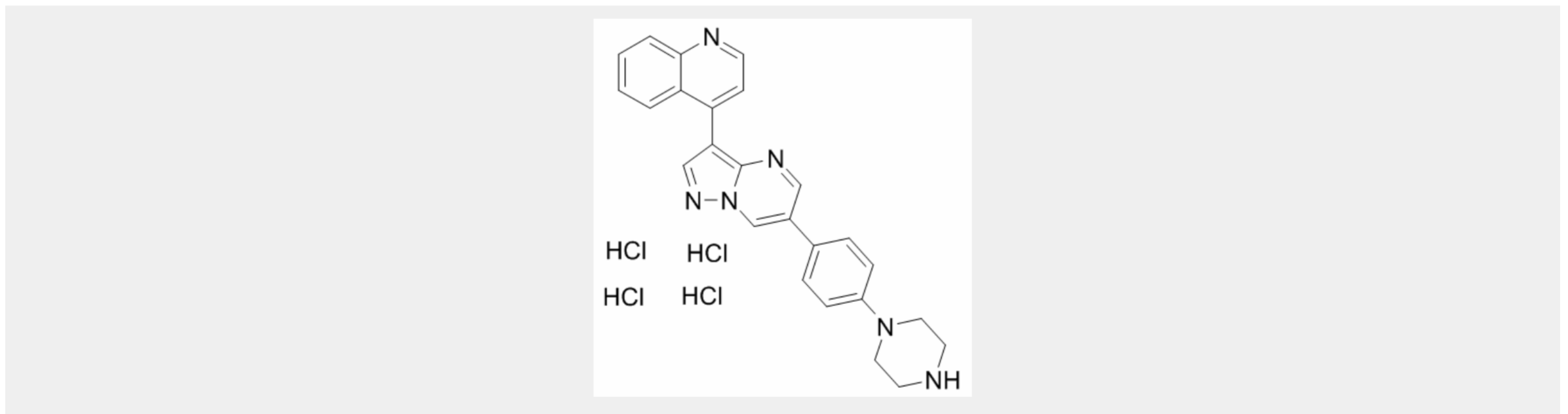
## Product Description

LDN193189 hydrochloride 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- $\beta$  type I receptors ALK4, ALK5 and ALK7 ( $IC_{50}$ ≥500 nM).

IC50 & Target: IC50: 5 nM (ALK2), 30 nM (ALK3)<sup>[1]</sup>

**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- $\beta$  signaling ( $IC_{50}$  for TGF- $\beta$   $\geq$ 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- $\beta$  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<sup>R206H</sup> or ALK2<sup>Q207D</sup> 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<sup>[1]</sup>.

**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 ( $1 \times 10^6$  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<sup>[2]</sup>. 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<sup>[3]</sup>.



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!