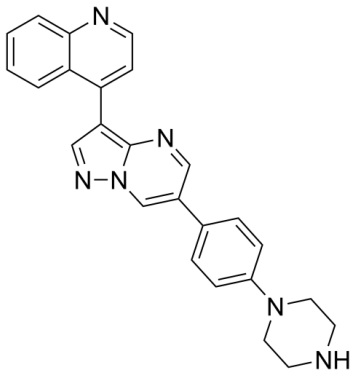
Data Sheet

Product Name:	LDN193189
Cat. No.:	CS-0669
CAS No.:	1062368-24-4
Molecular Formula:	$C_{25}H_{22}N_6$
Molecular Weight:	406.48
Target:	TGF-β Receptor
Pathway:	TGF-beta/Smad
Solubility:	DMSO : 12 mg/mL (29.52 mM; ultrasonic and adjust pH to 2 with HCl); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

LDN193189 is a potent selective **BMP type I receptor** inhibitor. LDN-193189 efficiently inhibits transcriptional activity of the BMP type I receptors **ALK2** and **ALK3** with **IC_{50}** values of 5 nM and 30 nM, respectively. LDN-193189 can be used for the research of bone morphogenetic protein signalling, such as fibrodysplasia ossificans progressiva[1][2][3]. IC50 & Target:IC50: 5 nM (ALK2), 30 nM (ALK3)[1] **In Vitro:**LDN-193189 efficiently inhibits transcriptional activity of the BMP type I receptors ALK2 and ALK3 with IC_{50} values of 5 nM and 30 nM, respectively[1].

LDN-193189 has weake effects on activin and the TGF-β type I receptors ALK4, ALK5 and ALK7 with IC_{50} values of ≥ 500 nM[1].

LDN-193189 binds ActRIIA with K_d value of 14 nM[2].

LDN-193189 (0.5 μM; 30 min) targets GDF8 induced Smad2/3 signaling and repression of myogenic transcription factors[2].

LDN-193189 (0.05, 0.5, 5 μM) efficiently inhibits GDF8 induced Smad3/4 reporter gene activity[2].

LDN-193189 (0-5 μM) rescues myogenesis in myoblasts treated with GDF8[2]. **In Vivo:**LDN-193189 (i.p.; 3 mg/kg; daily; for 35 days) might affect the interaction between breast cancer cells and the bone environment[3].

LDN-193189 (i.p.; 3 mg/kg; single) shows a reduction in ectopic ossification and functional impairment[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay:LDN193189 is prepared in 2% (wt/vol) (2-hydroxypropyl)-β-cyclodextrin in PBS, pH 7.4[1].[1]Mouse PASMCs grown are transiently transfected to 50% confluence in six-well plates with 0.3 μg Id1promoter luciferase reporter construct (BRE-Luc) in combination with 0.6 μg of plasmid expressing constitutively active forms of BMP type I receptors (caALK2, caALK3 or caALK6). For both reporter plasmids, 0.2 μg of pRL-TKRenilla luciferase are used to control for transfection efficiency. PASMCs are incubated with LDN193189 (2 nM-32 μM) or vehicle starting 1 h after transfection. Cell extracts are harvested and quantified relative promoter activity by the ratio of firefly to Renilla luciferase activity with the dual luciferase assay kit. **Animal Administration:**[2][3]Mice[2]
In the first experiment, SCID mice are implanted with MDA-PCa-118b tumors. After 7 days when tumors reached measurable sizes, mice are injected with LDN193189 (3 mg/kg) or with vehicle intraperitoneally twice a day. Tumor sizes and body weights are measured weekly. Mice are injected with calcein at three days and one day prior to sacrifice. Blood is collected and tumors are weighed. A portion of the tumors are fixed in formaldehyde for micro-computed tomography (microCT), using EVS CT, or further decalcified for bone histomorphometric analysis, using OsteoMeasure Analysis System, or flash frozen for RNA preparation. Osteocalcin in the mouse serum is determined by ELISA. In the second experiment, PCa-118b tumors are first digested with Accumax, and the isolated cells are plated overnight, resuspended in Matrigel in 1:1 ratio, and injected into SCID mice (1×10^6 cells/mouse) subcutaneously. Mice are treated with LDN193189 five days post-injection.
Rats[3]

Male Sprague-Dawley (SD) rats, 8 weeks of age, weighing 200-220 g, are purchased from Nanjing Medical University animal center. Rats are randomly assigned to one of seven experiment groups (n=6 per group). Rats are housed with free access to food and water under a natural 12/12 h day/night cycle. The Monocrotaline is administered (60 mg/kg) to rats by subcutaneous injection into the back region. The animal's lungs are harvested at 28th day of the study after hemodynamic assessment. The UK-92480 group received daily intragastric administration of UK-92480 after the administration of MCT (60 mg/kg). The LDN193189 group received daily intragastric administration of UK-92480 (50 mg/kg) and intraperitoneal injection of LDN193189 (10 mg/kg). In other groups, the same volume saline is given.

References:

[1]. Yu PB, et al. BMP type I receptor inhibition reduces heterotopic [corrected] ossification. Nat Med, 2008, 14(12), 1363-1369.

[2]. Daniel Horbelt, et al. Small molecules dorsomorphin and LDN-193189 inhibit myostatin/GDF8 signaling and promote functional myoblast differentiation. J Biol Chem. 2015 Feb 6;290(6):3390-404.

[3]. Julien Vollaire, et al. The Bone Morphogenetic Protein Signaling Inhibitor LDN-193189 Enhances Metastasis Development in Mice. Front Pharmacol. 2019 Jun 19;10:667.

CAIndexNames:

Quinoline, 4-[6-[4-(1-piperazinyl)phenyl]pyrazolo[1,5-a]pyrimidin-3-yl]-

SMILES:

C1(C2=C3N=CC(C4=CC=C(N5CCNCC5)C=C4)=CN3N=C2)=CC=NC6=CC=CC=C16

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA