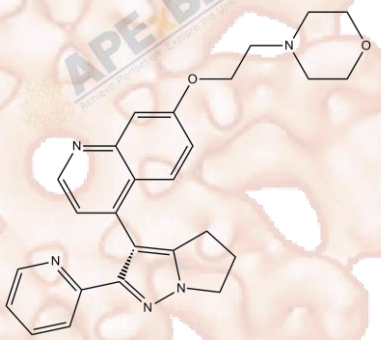
Product Data Sheet

LY2109761



Cat. No.:	A8464
CAS No.:	700874-71-1
Formula:	C26H27N5O2
M.Wt:	441.52
Synonyms:	
Target:	TGF-β / Smad Signaling
Pathway:	TGF-βR1(ALK5)
Storage:	Store at -20°C

Solvent & Solubility

In Vitro

⩾22.1 mg/mL in DMSO; insoluble in H2O; insoluble in EtOH

Preparing Stock Solutions

Mass / Solvent / Concentration	1mg	5mg	10mg
1 mM	2.2649 mL	11.3245 mL	22.6490 mL
5 mM	0.4530 mL	2.2649 mL	4.5298 mL
10 mM	0.2265 mL	1.1325 mL	2.2649 mL

Please refer to the solubility information to select the appropriate solvent.

Biological Activity

Shortsummary	TβRI/II kinase inhibitor
IC_{50} & Target	38 nM (Ki) (TβRI), 300 nM (Ki) (TβRII)

In Vitro

Cell Viability Assay

Cell Line:	Human cell MDA PCa 2b, PC-3 lines.
Preparation method：	The solubility of this compound in DMSO is <10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.
Reacting conditions:	24h; 4 μM

	Applications:	A crucial step in the transduction of TGF-β 1 signals is the phosphorylation of receptor-activated Smad2 and Smad3. We thus assessed the phosphorylation of Smad2 in lysates of MDA PCa 2b cells, PC-3 cells, and PMOs treated with rhTGF- β1. We found that TGF-β1 induces phosphorylation of Smad2 in PC-3 cells and PMOs but not in MDA PCa 2b cells. Further, treatment with LY2109761 reverses the Smad2 phosphorylation induced by rhTGF-β1. In other words, LY2109761 inhibits TGF-β1–induced Smad2 activation in PC-3 cells and PMOs.
In Vivo	**Animal experiment**	
	Animal models:	Male SCID mice
	Dosage form:	200 mg/kg/day; oral taken
	Applications:	After 3 weeks of treatment, X-ray analysis of the vehicle control group revealed two broken bones and loss of 30%–70% of the radiopaque areas in the tumor-bearing bones. MRI analysis showed a significantly smaller tumor volume in the treated group than in the controls (p =0.012). Micro-CT analysis of the tumor-bearing bones of the controls and treated mice demonstrated significantly lower BV (p=0.00043), BMC (p =0.000132), and BMD (p = 0.000085) in the control mice. Furthermore, BV, BMC, and BMD in the treated group were restored to values found in the normal (uninjected) femurs, which supports the efficacy of treatment. Finally, bone histomorphometric analysis demonstrated that LY2109761 inhibited PC-3-induced activation of osteoclasts.
	Other notes:	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Product Citations

1. Song Y, Chen Y, et al. "Resveratrol Suppresses Epithelial-Mesenchymal Transition in GBM by Regulating Smad-Dependent Signaling." Biomed Res Int. 2019 Apr 7;2019:1321973.PMID:31119150

2. Yang H, Li W, et al. "Regulatory role of miR-18a to CCN2 by TGF-β1 signaling pathway in pulmonary injury induced by nano-SiO(2)." Environ Sci Pollut Res Int. 2017 Oct 24.PMID:29067610

3. Singh SK, Fiorelli R, et al. "Post-translational Modifications of OLIG2 Regulate Glioma Invasion through the TGF-β Pathway." Cell Rep. 2016 Jul 26;16(4):950-66.PMID:27396340

4. Llobet-Navas, David, et al. "The miR-424/503 cluster reduces CDC25A expression during cell cycle arrest imposed by TGFβ in mammary epithelial cells." Molecular and Cellular Biology (2014): MCB-00611.PMID:25266660

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References

[1] Wan X, Li Z G, Yingling J M, et al. Effect of transforming growth factor beta (TGF-β) receptor I kinase inhibitor on prostate cancer bone growth[J]. Bone, 2012, 50(3): 695-703.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most APExBIO products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

APExBIO Technology

www.apexbt.com

7505 Fannin street, Suite 410, Houston, TX 77054.

Tel: +1-832-696-8203 | Fax: +1-832-641-3177 | Email: info@apexbt.com