

# Small Molecules

LY364947

Activin/BMP/TGF- $\beta$  pathway inhibitor;  
Inhibits ALK5

Catalog # 72592

5 mg



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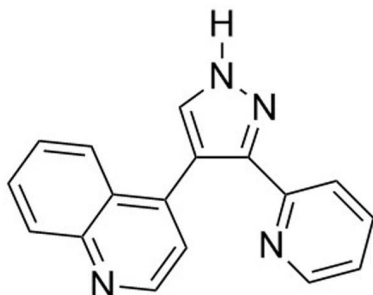
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## Product Description

LY364947 is a selective inhibitor of Activin/NODAL/TGF $\beta$  pathway that inhibits ALK5 (Sawyer et al.). Transforming growth factor- $\beta$  (TGF $\beta$ ) superfamily ligands signal through a cell surface heteromeric complex involving type I (TGF $\beta$ RI) and type II (TGF $\beta$ RII) receptors. Downstream signal transduction is mediated by the TGF $\beta$ RI kinase domain through the phosphorylation of SMAD proteins. LY364947 is a selective inhibitor of the TGF $\beta$ RI ALK5 ( $IC_{50}$  = 59 nM; Sawyer et al.). LY364947 less effectively inhibits TGF $\beta$ RII ( $IC_{50}$  = 400 nM), p38 MAPK ( $IC_{50}$  = 740 nM), and mixed lineage kinase-7 (MLK-7;  $IC_{50}$  = 1,400 nM; Li et al., 2006; Sawyer et al.).

Molecular Name:	LY364947
Alternative Names:	E-616451; HTS 466284; TGF- $\beta$ RI Kinase Inhibitor
CAS Number:	396129-53-6
Chemical Formula:	C <sub>17</sub> H <sub>12</sub> N <sub>4</sub>
Molecular Weight:	272.3 g/mol
Purity:	≥ 98%
Chemical Name:	4-(3-Pyridin-2-yl)(1H)-pyrazol-4-yl quinoline
Structure:	



## Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. For product expiry date, please contact techsupport@stemcell.com.
Solubility:	· DMSO ≤ 3.6 mM For example, to prepare a 1 mM stock solution in DMSO, resuspend 1 mg in 3.67 mL of fresh DMSO.

Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application.

Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

## Published Applications

### REPROGRAMMING

- In combination with valproic acid, can replace SOX2 in reprogramming of mouse embryonic fibroblasts transduced with OCT4, KLF4 and c-MYC (Ichida et al.).

### DIFFERENTIATION

- Blocks chondrogenesis induced by mechanical load in human mesenchymal stem cells (Li et al., 2010).
- Restores the hematopoietic potential of mouse para-aortic splanchnopleural cells deficient for the Evi-1 transcription factor (Sato et al.).
- Impairs definitive endoderm differentiation competence in human embryonic stem (ES) cells (Jaremko et al.).
- Blocks TGF- $\beta$ -induced endothelial-to-mesenchymal transition of NMuMg mammary epithelial cells or mouse ES cell-derived endothelial cells (Peng et al.; Kokudo et al.).

### CANCER RESEARCH

- Suppresses colony-forming ability of mouse and human leukemia-initiating cells cultured with OP-9 stromal cells, and, when combined with imatinib, reduces lethality in a mouse model of chronic myeloid leukemia (Naka et al.).
- Reduces invasiveness of MDA-MB-231 breast cancer cells in a matrigel invasion assay (Shiou et al.).

## References

- Ichida JK et al. (2009) A small-molecule inhibitor of *tgf*-Beta signaling replaces *sox2* in reprogramming by inducing *nanog*. *Cell Stem Cell* 5(5): 491–503.
- Jaremko KL & Marikawa Y. (2013) Regulation of developmental competence and commitment towards the definitive endoderm lineage in human embryonic stem cells. *Stem Cell Res* 10(3): 489–502.
- Kokudo T et al. (2008) Snail is required for TGFbeta-induced endothelial-mesenchymal transition of embryonic stem cell-derived endothelial cells. *J Cell Sci* 121(20): 3317–24.
- Li H et al. (2006) Dihydropyrrlopyrazole transforming growth factor-beta type I receptor kinase domain inhibitors: a novel benzimidazole series with selectivity versus transforming growth factor-beta type II receptor kinase and mixed lineage kinase-7. *J Med Chem* 49(6): 2138–42.
- Li Z et al. (2010) Mechanical load modulates chondrogenesis of human mesenchymal stem cells through the TGF-beta pathway. *J Cell Mol Med* 14(6A): 1338–46.
- Naka K et al. (2010) TGF-beta-FOXO signalling maintains leukaemia-initiating cells in chronic myeloid leukaemia. *Nature* 463(7281): 676–80.
- Peng S-B et al. (2005) Kinetic characterization of novel pyrazole TGF-beta receptor I kinase inhibitors and their blockade of the epithelial-mesenchymal transition. *Biochemistry* 44(7): 2293–304.
- Sato T et al. (2008) Evi-1 promotes para-aortic splanchnopleural hematopoiesis through up-regulation of GATA-2 and repression of TGF- $\beta$  signaling. *Cancer Sci* 99(7): 1407–13.
- Sawyer JS et al. (2003) Synthesis and Activity of New Aryl- and Heteroaryl-Substituted Pyrazole Inhibitors of the Transforming Growth Factor- $\beta$  Type I Receptor Kinase Domain. *J Med Chem* 46(19): 3953–3956.
- Shiou S-R et al. (2006) Smad4-dependent regulation of urokinase plasminogen activator secretion and RNA stability associated with invasiveness by autocrine and paracrine transforming growth factor-beta. *J Biol Chem* 281(45): 33971–81.

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