



Product Specification Sheet

Product Name: LY2157299**Catalog Number:** C5921-2 (powder)
C5921-2s (10mM in DMSO)**Package Size:** 2 mg**Technical information:****Chemical Formula:** C₂₂H₁₉N₅O**CAS #:** 700874-72-2, 912477-03-3**Molecular Weight:** 369.42**Purity:** >98%**Formulation:** Off-white**Solubility:** Soluble in DMSO up to 50 mM**Chemical Name:** 4-[2-(6-Methyl-pyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]-quinoline-6-carboxylic acid amide**Storage:** Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.**Handling:**

- For C5921-2 (powder), add 0.541 mL of DMSO to make 10 mM solution.
- For C5921-2s, briefly spin the vial at 500 rpm inside a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity: LY2157299, a specific and potent TGF- β receptor (T β R) inhibitor that competitively binds to the active site of its kinase domain¹, inhibiting TGF- β -mediated SMAD2 phosphorylation/activation and down streaming signaling.

LY2157299 inhibited hematopoietic suppression in primary hematopoietic stem cells, such that it improved anemia in a TGF- β overexpressing transgenic mouse model, and stimulated hematopoiesis from primary MDS bone marrow specimens². Daily oral administration of LY2157299 in patients with advanced/metastatic cancer was tolerated well with an expected pharmacokinetic profile^{3,4}.

Reference:

1. Yingling, J. et al. Targeting the TGF- β RI kinase with LY2157299: A PK/PD-driven drug discovery and clinical development program. Proc Amer Assoc Cancer Res, 46, SY13-2, (2005).
2. Zhou L., et al. Reduced SMAD7 leads to overactivation of TGF-beta signaling in MDS that can be reversed by a specific inhibitor of TGF-beta receptor I kinase. Cancer Res. 71(3):955-63. (2011)
3. Bueno, L., et al. Semi-mechanistic modelling of the tumour growth inhibitory effects of LY2157299, a new type I receptor TGF-b kinase antagonist, in mice. Eur J Cancer., 44(1):142-150, (2008).
4. E. Calvo-Aller et al. First human dose escalation study in patients with metastatic malignancies to determine safety and pharmacokinetics of LY2157299, a small molecule inhibitor of the transforming growth





factor-beta receptor I kinase. J Clin Oncol 26: (May 20 suppl; abstr 14554), (2008)

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