Product Specification Sheet

Product Name: LY2157299

Catalog Number: C5921-2 (powder)
C5921-2s (10mM in DMSO)

Package Size: 2 mg

Technical information:

Chemical Formula:	$C_{22}H_{19}N_5O$
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 (TβR) inhibitor that competitively binds to the active site of its kinase domain[1], inhibiting TGF-β-mediated SMAD2 phosphorylation/activation and down streaming signaling.

LY2157299 inhibited hematopoetic 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 specimens[2]. 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-ß 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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