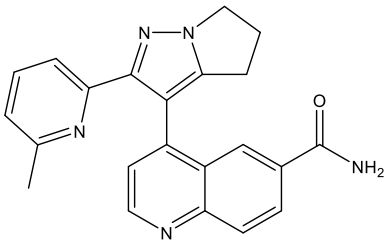
Catalog # 10-4110
Galunisertib

CAS# 700874-72-2

4-[2-(6-Methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]quinoline-6-carboxamide; LY2157299

Lot # FBS1099



Galunisertib is a TGF-β kinase (ALK5) antagonist.[1] It stimulated hematopoiesis from primary myelodysplastic syndrome bone marrow specimens via downregulation of SMAD2 phosphorylation.[2] It has been in clinical trials for treatment of various cancers.[3-5] Galunisertib has more recently been used to enhance the anti-neuroblastoma activity of anti-GD2 antibody Dinutuximab with natural killer cells[6] and preserved the function of in vitro expanded natural killer cells in AML and colon cancer models[7]. Galunisertib reversed TGFβ and regulatory T cell mediated suppression of human T cell proliferation. In combination with PD-L1 blockade, it resulted in improved tumor growth inhibition and complete regressions in colon carcinoma models.[8]

1) Bueno *et al.* (2008), *Semi-mechanistic modelling of the tumour growth inhibitory effects of LY2157299, a new type I receptor TGF-β kinase antagonist, in mice;* Eur.J.Cancer **44** 142
2) Zhou *et al.* (2011), *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** 955
3) Rodon *et al*. (2015), *First-in-human dose study of the novel transforming growth factor-b-receptor I kinase inhibitor LY2157299 monohydrate in patients with advances cancer and glioma*; Clin.Cancer Res. **21** 553
4) Herbertz *et al*. (2015), *Clinical development of galunisertib (LY2157299 monohydrate), a small molecule inhibitor lof transforming growth factor-beta signaling pathway*; Drug Des.Devel.Ther. **9** 4479
5) Brandes *et al*. (2016), *A Phase II randomized study of galunisertib monotherapy or galunisertib plus lomustine compared with lomustine monotherapy in patients with recurrent glioblastoma*; Neuro.Oncol. **18** 1146
6) Tran *et al*. (2017), *TGFβR1 Blockade with Galunisertib (LY2157299 Enhances Anti-Neuroblastoma Activity of the Anti-GD2 Antibody Dinutuximab (ch14.18) with Natural Killer Cells*; Clin.Cancer Res. **23** 804
7) Otegbeye *et al*. (2018), *Inhibiting TGF-beta signaling preserves the function of highly activated, in vitro expanded natural killer cells in AML and colon cancer models*; PLoS One **13** e0197008
8) Holmgaard *et al*. (2018), *Targeting the TGFβ pathway with galunisertib, a TGFβRI small molecule inhibitor, promotes anti-tumor immunity leading to durable, complete response, as monotherapy and in combination with checkpoint blockade*; J.Immunother.Cancer **6** 47

PHYSICAL DATA

Molecular Weight:	369.43
Molecular Formula:	$C_{22}H_{19}N_5O$
Purity:	>98%
	NMR: (Conforms)
Solubility:	Soluble in DMSO (25 mg/ml)
Physical Description:	White solid
Storage and Stability:	Store as supplied at -20º for up to 1 year from the date of purchase. Store solutions at -20ºC for up to 1 month.

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