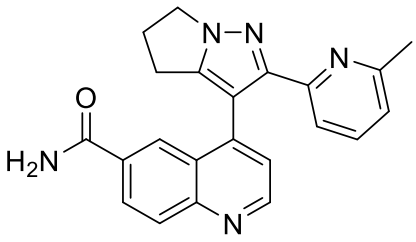
Product data sheet

MedKoo Cat#: 205520 Name: Galunisertib CAS#: 700874-72-2 Chemical Formula: $C_{22}H_{19}N_5O$ Exact Mass: 369.15896 Molecular Weight: 369.42	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Galunisertib, also known as LY2157299, is a novel, selective small molecule transforming growth factor beta receptor (TGF-βR) kinase inhibitor. LY2157299 inhibited HCC cell migration on Laminin-5, Fibronectin, Vitronectin, Fibrinogen and Collagen-I and de novo phosphorylation of pSMAD2. LY2157299 inhibited HCC migration and cell growth independently of the expression levels of TGF-βRII.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	24.0	65.0

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.71 mL	13.53 mL	27.07 mL
5 mM	0.54 mL	2.71 mL	5.41 mL
10 mM	0.27 mL	1.35 mL	2.71 mL
50 mM	0.05 mL	0.27 mL	0.54 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Wang Z, Liu Q, Risu N, Fu J, Zou Y, Tang J, Li L, Liu H, Zhou G, Zhu X. Galunisertib enhances chimeric antigen receptor-modified T cell function. Eur J Histochem. 2020 Jun 19;64(s2):3122. doi: 10.4081/ejh.2020.3122. PMID: 32705856; PMCID: PMC7388644.

In vivo study

1. Yingling JM, McMillen WT, Yan L, Huang H, Sawyer JS, Graff J, Clawson DK, Britt KS, Anderson BD, Beight DW, Desaiah D, Lahn MM, Benhadji KA, Lallena MJ, Holmgaard RB, Xu X, Zhang F, Manro JR, Iversen PW, Iyer CV, Brekken RA, Kalos MD, Driscoll KE. Preclinical assessment of galunisertib (LY2157299 monohydrate), a first-in-class transforming growth factor-β receptor type I inhibitor. Oncotarget. 2017 Dec 31;9(6):6659-6677. doi: 10.18632/oncotarget.23795. PMID: 29467918; PMCID: PMC5805504.

7. Bioactivity
Biological target:

TGF-β receptor type I (TGF-βRI) kinase inhibitor with an IC50 of 56 nM.

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In vitro activity

The combination of a small molecule inhibitor of TGF-β receptor I, Galunisertib, and CAR T cells was used to explore whether Galunisertib could enhance CAR T cell function against solid tumor cells. In vitro experiments showed Galunisertib could significantly enhance the specific cytotoxicity of both CD133- and HER2-specific CAR T cells. However, Galunisertib had no direct killing effect on target cells. Galunisertib significantly increased the cytokine secretion of CAR T cells and T cells that do not express CAR (Nontransfected T cells). Galunisertib did not affect the proliferation of T cells, the antigen expression on target cells and CD69 on CAR T cells. It was found that TGF-β was secreted by T cells themselves upon activation, and Galunisertib could reduce TGF-β signaling in CAR T cells.

Reference: Eur J Histochem. 2020 Jun 19; 64(Suppl 2): 3122. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7388644/

In vivo activity

The in vivo antitumor efficacy of galunisertib was evaluated using a dose of 75 mg/kg administered twice daily by oral gavage, the dosing schedule defined by the PK/PD profile described in the pSMAD inhibition assays (Figure (Figure4).4). Monotherapy anti-tumor activity of galunisertib was evaluated in three independent models; the immune competent 4T1 syngenic murine breast cancer model, the MX1 human xenograft breast cancer model, and the Calu6 human xenograft lung cancer model. In each of these established tumor models, galunisertib monotherapy resulted in significant tumor growth delay (Figure 7A, 7B, 7C, and and7D).7D). For MX1, galunisertib monotherapy resulted in tumor growth delay of 10.3±4.3 days (1500 mm3 crossing time, $p = 0.014$) (Figure (Figure7A)7A) and for Calu6 galunisertib monotherapy resulted in tumor growth delay of 8.3 +/− 2.6 days (500 mm3 crossing time, $p = 0.034$) (Figure (Figure7B);7B); for 4T1, galunisertib monotherapy resulted in a tumor growth delay of 13±2.4 days (500 mm3 crossing time, $p < 0.01$ by repeated measures analysis) and a survival advantage of 4.5 days ($p = 0.01$) (Figure 7C, 7D), demonstrating the antitumor activity of the compound in traditional preclinical tumor models.

Reference: Oncotarget. 2018 Jan 23; 9(6): 6659–6677. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5805504/