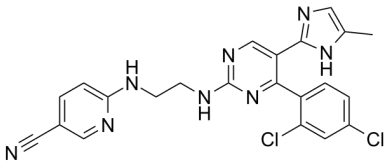
# CHIR-99021(CT99021)

Catalog Number: C252917

OrganRegen, INC.
*Creating Solutions for Organoid Cultures*

## DESCRIPTION

| | | | |
|---|---|---|---|
| Background | CHIR-99021 is a potent and selective GSK-3α/β inhibitor with $IC_{50}$s of 10 nM and 6.7 nM. Laduviglusib shows >500-fold selectivity for GSK-3 over CDC2, ERK2 and other protein kinases. Laduviglusib is also a potent Wnt/β-catenin signaling pathway activator. Laduviglusib enhances mouse and human embryonic stem cells self-renewal. Laduviglusib induces autophagy[1][2][3]. | | |
| Alias | Laduviglusib; CT99021 | | |
| M. W t | 465.34 | | |
| Formula | $C_{22}H_{18}C_{l2}N_8$ | | |
| CAS No | 252917-06-9 | | |
| Storage | Powder | -20°C | 3 years |
| | | 4°C | 2 years |
| | In solvent | -80°C | 6 months |
| | | -20°C | 1 month |
| Solubility | DMSO | 16.67 mg/mL(35.82 mM) | |
| | $H_2O$ | < 0.1 mg/mL(insoluble) | |



$C_{22}H_{18}C_{l2}N_8$

## BIOLOGICAL ALTIVITY

**In Vitro**

CHIR-99021 inhibits human GSK-3β with $K_i$ values of 9.8 nM[1]. Laduviglusib is a small organic molecule that inhibits GSK3α and GSK3β by competing for their ATP-binding sites.In vitro kinase assays reveal that Laduviglusib specifically inhibits GSK3β ($IC_{50}$=~5 nM) and GSK3α ($IC_{50}$=~10 nM), with little effect on other kinases[4]. In the presence of Laduviglusib the viability of the ES-D3 cells is reduced by 24.7% at 2.5 μM, 56.3% at 5 μM, 61.9% at 7.5 μM and 69.2% at 10 μM Laduviglusib with an $IC_{50}$ of 4.9 mm[2].

**In Vivo**

In ZDF rats, a single oral dose of Laduviglusib (16 mg/kg or 48 mg/kg) rapidly lowers plasma glucose, with a maximal reduction of nearly 150 mg/dl 3-4 h after administration[1]. Laduviglusib (2 mg/kg) given once, 4 h before irradiation, significantly improves survival after 14.5 Gy abdominal irradiation (ABI). Laduviglusib treatment significantly blocks crypt apoptosis and accumulation of p-H2AX$^+$ cells, and improves crypt regeneration and villus height. Laduviglusib treatment increases Lgr5$^+$ cell survival by blocking apoptosis, and effectively prevents the reduction of Olfm4, Lgr5 and CD44 as early as 4 h[5].

## REFERENCES


[1]. Ring DB, et al. Selective glycogen synthase kinase 3 inhibitors potentiate activation of glucose transport and utilization in vitro and in vivo. Diabetes. 2003 Mar;52(3):588-95.

[2]. Naujok O, et al. Cytotoxicity and activation of the Wnt/beta-catenin pathway in mouse embryonic stem cells treated with four GSK3 inhibitors.BMC Res Notes. 2014 Apr 29;7:273.

[3]. Ye S, et al. Pleiotropy of glycogen synthase kinase-3 inhibition by CHIR99021 promotes self-renewal of embryonic stem cells from refractory mouse strains. PLoS One. 2012;7(4):e35892.

[4]. Bennett CN, et al. Regulation of Wnt signaling during adipogenesis. J Biol Chem. 2002 Aug 23;277(34):30998-1004.

[5]. Wang X, et al. Pharmacologically blocking p53-dependent apoptosis protects intestinal stem cells and mice from radiation. Sci Rep. 2015 Apr 10;5:8566.