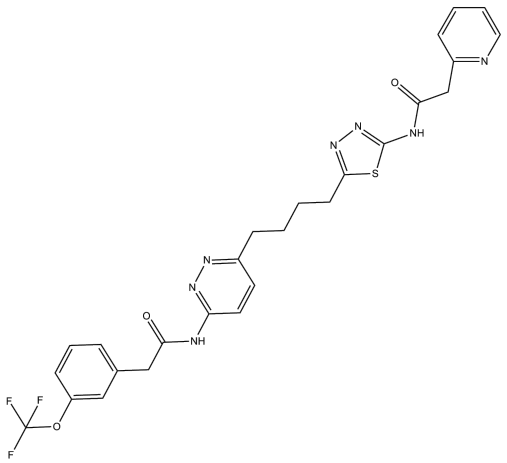
Product Data Sheet

Product Name: CB-839
Cat. No.: GC15227

Chemical Properties

Cas. No.	1439399-58-2		
Chemical Name	2-(pyridin-2-yl)-N-(5-(4-(6-(2-(3-(trifluoromethoxy)phenyl)acetamido)pyridazin-3-yl)butyl)-1,3,4-thiadiazol-2-yl)acetamide		
SMILES	FC(F)(F)OC1=CC(CC(NC2=NN=C(CCCCC3=NN=C(NC(CC4=NC=CC=C4)=O)S3)C=C2)=O)=CC=C1		
Formula	$C_{26}H_{24}F_3N_7O_3S$	M.Wt	571.57
Solubility	≥ 28.6mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

Cell lines TNBC cell lines HCC1806 and MDA-MB-231, T47D cell line

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Preparation method	For viability assays, all cell lines were treated with Telaglenastat at the indicated concentrations for 72 hours in duplicate wells and analyzed for antiproliferative effects using Cell Titer Glo.
Reacting condition	1μM, 72 hours
Applications	Telaglenastat treatment showed a potent effect on the proliferation of HCC1806 and MDA-MB-231 cells with the IC_{50} of 20–55nM. Telaglenastat (1μM) inhibited the metabolism of glutamine, the rates of glutamine consumption and glutamate production in HCC1806 and T47D cell lines. TNBC cell lines exhibited greater sensitivity as measured by the extent of cell growth or cell loss following treatment with 1μM Telaglenastat for 72 hours.

Animal experiment [1]:

Animal models	Scid/Beige mice bearing orthotopically implanted HCC1806 tumors, Patient-derived TNBC and JIMT-1 cell line xenograft models
Dosage form	Oral administration; 200mg/kg; twice daily; 28 days
Application	In primary patient-derived TNBC mouse model, oral dosing of single agent Telaglenastat (200mg/kg twice daily) suppressed tumor growth. In the mouse JIMT-1 xenograft model, oral dosing of Telaglenastat alone (200mg/kg twice daily) resulted in 54% tumor growth inhibition (TGI). Combination of Telaglenastat (200mg/kg, p.o.) with paclitaxel (10mg/kg, p.o.) largely suppressed the regrowth of the tumors resulting in a TGI relative to vehicle control of 100%.

Caution: Product has not been fully validated for medical applications. For research use only.
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Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

References:
[1]. Gross M I, Demo S D, Dennison J B, et al. Antitumor activity of the glutaminase inhibitor CB-839 in triple-negative breast cancer[J]. Molecular cancer therapeutics, 2014, 13(4): 890-901.

Background

Telaglenastat (CB-839) is a reversible, orally bioavailable glutaminase 1 (GLS1) inhibitor that induces autophagy and has antitumor activity[1]. Compared to GLS2, Telaglenastat selectively inhibits the GLS1 splice variants KGA (kidney-type glutaminase) and GAC (glutaminase C)[2]. The IC_{50} values of Telaglenastat for endogenous glutaminase in mouse kidney and brain are 23nM and 28nM, respectively.

Telaglenastat(0.1-1000nM; 72 hours) had antiproliferative activity in HCC1806 and MDA-MB-231 cells with IC_{50}s of 49nM and 26nM, respectively[1].Telaglenastat (1μM; 72 hours) activated caspase 3/7 and induced apoptosis in MDA-MB-231 and HCC1806 cells[1].

Telaglenastat (200mg/kg; p.o.; twice daily for 28 days) had antitumor activity in mice xenograft models of TNBC[1].

References:

[1]. Gross MI, et al. Antitumor activity of the glutaminase inhibitor CB-839 in triple-negative breast cancer. Mol Cancer Ther. 2014 Apr;13(4):890-901.

[2]. Biancur DE, et al. Compensatory metabolic networks in pancreatic cancers upon perturbation of glutaminemetabolism. Nat Commun. 2017 Jul 3;8:15965.

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