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GLS1 Inhibitor III, CB-839 - CAS 1439399-58-2 - Calbiochem Cell-permeable, orally available, potent, selective & non-competitive GLS1 inhibitor. Reduces glutamine consumption & glutamate secretion, and induces apoptosis.

Art. ID	SAF-5337170001
Unit	EA

Description

A cell-permeable thiadiazolyl-butyl-pyridazinyl compound that selectively inhibits GLS1 (IC50 = 23 nM &amp,amp,amp,amp,amp,amp,amp, 28 nM, respectively, using murine kidney and brain homogenates), but not GLS2/LGA (up to 5 &amp,amp,amp,amp,amp,amp,micro,M using murine liver homogenates), glutaminase activity in a non-competitive manner, being more potent than the uncompetitive GLS1 inhibitor BPTES, but with much slower inhibition kinetics (IC50/preincubation time ~300 nM/1 min &amp,amp,amp,amp,amp,amp,amp, &amp,amp,amp,amp,amp,amp,amp, 50 nM/1 h for CB-839, 630 nM/1 min &amp,amp,amp,amp,amp,amp,amp, 700 nM/1 h for BPTES, 2 nM rhGAC aa 126-598) &amp,amp,amp,amp,amp,amp,amp, reversibility (Activity recovery t1/2&amp,lt,/sub> after free drug removal = 45 min/CB-839 &amp,amp,amp,amp,amp,amp,amp, &amp,lt,3 min/BPTES). CB-839 also displays higher antiproliferation potency than BPTES against triple negative breast cancer (TNBC) cultures (GI50 against MDA-MB-231 in 72 h = 19 nM vs. 2.4 &amp,amp,amp,amp,amp,amp,micro,M with BPTES, GI50 against HCC1806 in 72 h = 55 nM vs. 2.0 &amp,amp,amp,amp,amp,amp,micro,M with BPTES), while neither drug is effective against GLS1-independent growth of estrogen receptor-positive T47D even at 1 &amp,amp,amp,amp,amp,amp,micro,M concentration. Despite a fast clearance in mice (Plasma t1/2&amp,lt,/sub>3 tumor) except brain (~0.2 nmol/g) with most pronounced Glutamine buildup observed in tumor (5-fold) when compared to normal tissues (1- to 2.28-fold of of no treatment controls). Twice daily oral administration (200 mg/kg/12 h) is efficacious in suppressing the expansion of established tumor derived from HIMT-1 (by 54% in 35 d) and patient TNBC (by 59% in 28 d) and complete suppression of JIMT-1 tumor is seen when combined with 5 daily doses of Paclitaxel (10 mg/kg i.v., Cat. Nos. 580555 &amp,amp,amp,amp,amp,amp,amp, 580556) in the first 5 d of the treatment period., A cell-permeable, orally available thiadiazolyl-butyl-pyridazinyl compound that acts as a potent, selective, time-dependent, and slowly-reversible (t1/2 = 45 min at 25 C) inhibitor of glutaminase (IC50 = 45, 23 and 28 nM for rec hu-GAC, KGA and GAC, respectively). The inhibition appears to be non-competitive and allosteric. Exhibits anti-proliferative effects in HCC1806 and MDA-MB-231 triple-negative breast cancer cell lines (IC50 = 49 and 26 nM, respectively), but does not affect the viability of ER+/HER2-T47D cell line. Shown to reduce glutamine consumption (IC50 = 17 nM) and glutamate production (IC50 = 15 nM) rates in HCC1806 cells. Inhibits the growth of HCC1806 xenografts in mice (~200 mg/kg, p.o., b.i.d) and of JIMT-1 xenografts (200 mg/kg p.o., b.i.d), either alone or in combination with paclitaxel (10 mg/kg , 5 doses alternate days).Please note that the molecular weight for this compound is batch-specific due to variable water content. Please refer to the vial label or the certificate of analysis for the batch-specific molecular weight. The molecular weight provided represents the baseline molecular weight without water.

Text/Information	Analyte/Parameter	CAS number	Concentration/Value	Unit	Method	Source
	CB-839	[1439399-58-2]				