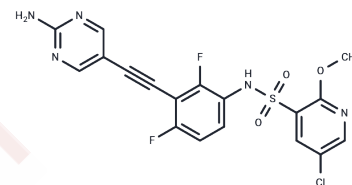


## GCN2iB

## Chemical Properties

CAS No. :	2183470-12-2
Formula:	C <sub>18</sub> H <sub>12</sub> ClF <sub>2</sub> N <sub>5</sub> O <sub>3</sub> S
Molecular Weight:	451.83
Storage:	Powder: -20°C for 3 years   In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



## Biological Description

Description	GCN2iB is an ATP-competitive inhibitor of serine/threonine protein kinase, stress-responsive kinase (GCN2), with IC <sub>50</sub> of 2.4 nM.
Targets(IC <sub>50</sub> )	Autophagy,PERK
In vitro	<p><b>METHODS:</b> HEK293 cells were treated with 4 nM to 4 μM Gcn2iB for 6 h in the presence or absence of Halofuginone (HF) treatment to explore the concentration-dependent effect of Gcn2iB on ISR activation.</p> <p><b>RESULTS</b> HF treatment resulted in increased levels of p-Gcn2, p-eIF2α, and Atf4, each of which decreased with increasing concentrations of Gcn2iB; p-Gcn2 induction decreased at 62.5 nM Gcn2iB or higher, and Atf4 induction decreased at 250 nM Gcn2iB; cells treated with Gcn2iB in the absence of HF exhibited a biphasic response to the induction of p-Gcn2, p-eIF2α, and Atf4, with increases in all three ISR markers observed in the range of 10 to 100 nM Gcn2iB; above 250 nM Gcn2iB, p-Gcn2 levels decreased to below those determined with vehicle, and Atf4 levels were not significantly induced; although Gcn2iB could inhibit Gcn2 stimulation by HF treatment, lower concentrations of Gcn2iB activated Gcn2 and the ISR in the absence of external stress. [1]</p>
In vivo	<p><b>METHODS:</b> HFD plus STZ-induced diabetic C57BL/6J mice were treated with intraperitoneal injection of GCN2iB (3 mg/kg) every other day for 6 weeks. At the end of the experiment, the mice were subjected to echocardiography.</p> <p><b>RESULTS</b> After GCN2iB treatment, the fasting blood glucose level (11.18 ± 1.44 vs. 17.42 ± 2.57 mmol/L) and body weight (28.94 ± 2.05 vs. 32.54 ± 1.49 g) of type 2 diabetic mice were significantly reduced; GCN2iB treatment had no effect on heart weight. Significant effects, but increased heart weight to body weight ratio; GCN2iB treatment significantly improved cardiac systolic function and increased left ventricular (LV) ejection fraction (EF). [2]</p>

## Solubility Information

Solubility	DMSO: 56.5 mg/mL (125.05 mM),Sonication is recommended. H <sub>2</sub> O: < 0.1 mg/mL (insoluble) (< 1 mg/ml refers to the product slightly soluble or insoluble)
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## A DRUG SCREENING EXPERT

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (2.21 mM), Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>
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### Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.2132 mL	11.0661 mL	22.1322 mL
5 mM	0.4426 mL	2.2132 mL	4.4264 mL
10 mM	0.2213 mL	1.1066 mL	2.2132 mL
50 mM	0.0443 mL	0.2213 mL	0.4426 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

Carlson KR, et al. Activation of Gcn2 by small molecules designed to be inhibitors. J Biol Chem. 2023 Apr;299(4):104595.

Xie S, Liu H, Zhu S, et al. Arsenic trioxide and p97 inhibitor synergize against acute myeloid leukemia by targeting nascent polypeptides and activating the ZAK $\alpha$ -JNK pathway. Cancer Gene Therapy. 2024: 1-12.

Yuan J, et al. Inhibition of GCN2 Alleviates Cardiomyopathy in Type 2 Diabetic Mice via Attenuating Lipotoxicity and Oxidative Stress. Antioxidants (Basel). 2022 Jul 16;11(7):1379.

Nakamura A, et al. Inhibition of GCN2 sensitizes ASNS-low cancer cells to asparaginase by disrupting the amino acid response. Proc Natl Acad Sci U S A. 2018 Aug 14;115(33):E7776-E7785.

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