

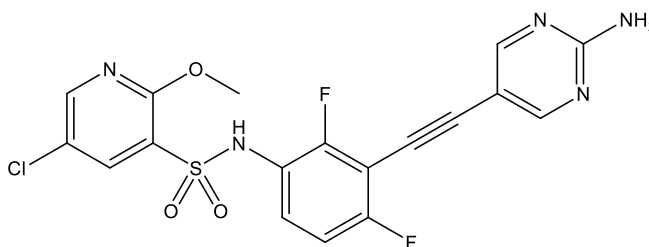
Catalog # 10-4332

GCN2iB

CAS# 2183470-12-2

N-[3-[2-(2-Aminopyrimidin-5-yl)ethynyl]-2,4-difluorophenyl]-5-chloro-2-methoxypyridine-3-sulfonamide

Lot # FBS5026



GCN2iB is a potent ($IC_{50} = 2.4$ nM) and highly selective (against 468 kinases) inhibitor of general control nonderepressible 2 (GCN2), an important kinase involved in amino acid homeostasis. It displayed robust antitumor activity in xenografts of ALL, AML, and pancreatic cancers in conjunction with asparaginase treatment.¹ GCN2iB alleviated adipocyte-mediated translation reducing their cytoprotective effect.² It exhibited protective effects in mouse models of cerebral ischemia.³ GCN2iB alleviated hepatic steatosis in obese mice⁴ and hyperglycemia and insulin resistance in diabetic mice⁵. It also protected against cardiac dysfunction in diabetic mice.⁶

- 1) Nakamura *et al.* (2018), *Inhibition of GCN2 sensitizes ASNS-low cancer cells to asparaginase by disrupting the amino acid response*; Proc. Natl. Acad. Sci. USA **115** E7776
- 2) Heydt *et al.* (2021), *Adipocytes disrupt the translational programme of acute lymphoblastic leukaemia to favour tumour survival and persistence*; Nat. Commun. **12** 5507
- 3) Shi *et al.* (2019), *GCN2 suppression attenuates cerebral ischemia in mice by reducing apoptosis and endoplasmic reticulum (ER) stress through the blockage of FoxO3a-regulated ROS production*; Biochem. Biophys. Res. Commun. **516** 285
- 4) Yuan *et al.* (2022), *Inhibition of GCN2 alleviates hepatic steatosis and oxidative stress in obese mice: Involvement of NRF2 regulation*; Redox Biol. **49** 102224
- 5) Yuan *et al.* (2022), *Genetic and pharmacological inhibition of GCN2 Ameliorates Hyperglycemia and Insulin Resistance in Type 2 Diabetic Mice*; Antioxidants (Basel) **11** 1584
- 6) Yuan *et al.* (2022), *Inhibition of GCN2 Alleviates Cardiomyopathy in Type 2 Diabetic Mice via Attenuating Lipotoxicity and Oxidative Stress*; Antioxidants (Basel) **11** 1379

PHYSICAL DATA

Molecular Weight:	451.83
Molecular Formula:	C ₁₈ H ₁₂ ClF ₂ N ₅ O ₃ S
Purity:	>98% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (>25 mg/ml)
Physical Description:	Off-white to cream solid
Storage and Stability:	Store as supplied at -20°C for up to 2 years from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 1 month.

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