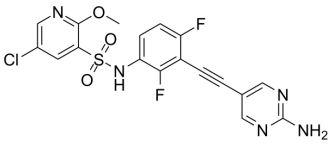
GCN2iB

Cat. No.:	HY-112654
CAS No.:	2183470-12-2
Molecular Formula:	$C_{18}H_{12}ClF_2N_5O_3S$
Molecular Weight:	452
Target:	Eukaryotic Initiation Factor (eIF); Autophagy
Pathway:	Cell Cycle/DNA Damage; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (110.62 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2124 mL	11.0619 mL	22.1239 mL
	5 mM	0.4425 mL	2.2124 mL	4.4248 mL
	10 mM	0.2212 mL	1.1062 mL	2.2124 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (3.69 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (3.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GCN2iB is an ATP-competitive inhibitor of a serine/threonine-protein kinase general control nonderepressible 2 (GCN2), with an IC_{50} of 2.4 nM.

IC_{50} & Target

IC50: 2.4 nM (GCN2)[1].

In Vitro

GCN2iB shows an IC_{50} value of 2.4 nM for GCN2 and potent cellular activity. In a panel of 468 kinases, only GCN2 shows >99.5% inhibition, and three kinases (MAP2K5, STK10, and ZAK) show >95%inhibition at 1 μM GCN2iB, demonstrating high kinase selectivity[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	In the antitumor activity study of the CCRF-CEM xenografts, ASNase or GCN2iB alone does not significantly affect tumor growth. Notably, a combination of ASNase and GCN2iB elicit potent antitumor activity (P=0.0002) with synergistic effects. In MV-4-11 and SU.86.86 xenografts, robust antitumor activity of the combination of GCN2iB and ASNase is observed with synergistic effect, respectively. ASNase/GCN2iB-treated tumors do not show significant growth even after drug cessation. The combination of ASNase and GCN2iB yield survival advantage compared with the vehicle treated control with synergistic effect[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Mice[1] A suspension of CCRF-CEM, HPB-ALL, MV-4-11, or SU.86.86 cells (1×10^7 cells/site) is subcutaneously injected into the right flanks of 6-week-old female SCID mice. Tumor volume is calculated as volume =$L\times l^2\times1/2$, where L represents the longest diameter across the tumor and l represents the corresponding perpendicular distance. Body weight is also measured. To assess the anti-tumor activity, mice with tumor mass ~200 mm^3 are sorted into treatment groups (N=5/group). The tumors are monitored and mice are euthanized when an endpoint is reached, or at the end of the study, whichever comes first. From the next day of randomization, GCN2 inhibitors (e.g., GCN2iB, 10 mpk, twice a day) or ASNase is orally or intraperitoneally administered to mice bearing the xenografts for 7 to 10 days, respectively. T/C (%), an index of anti-tumor activity, is calculated by comparing the mean change in tumor volume during the treatment period in the control and treated groups[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Discov. 2021 Oct 26;7(1):98.
- Cell Metab. 2023 Nov 11:S1550-4131(23)00385-6.
- Cell Metab. 2022 Aug 2;34(8):1151-1167.e7.
- Nat Cancer. 2022 Nov 21.
- Nat Commun. 2023 Aug 8;14(1):4758.

See more customer validations on www.MedChemExpress.com

REFERENCES

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

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA