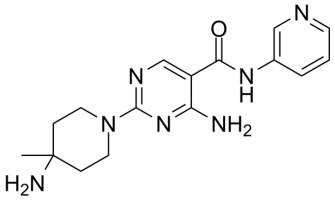
SHP2-IN-13

Cat. No.:	HY-149241
CAS No.:	2951854-02-5
Molecular Formula:	$C_{16}H_{21}N_7O$
Molecular Weight:	327.38
Target:	SHP2
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

SHP2-IN-13 is a highly selective and orally active SHP2 “tunnel site” allosteric inhibitor with an IC50 of 83.0 nM. SHP2-IN-13 has the potential for cancers bearing RTK oncogenic drivers and SHP2-related diseases research.

In Vitro

SHP2-IN-13 (compound 129) potently inhibits the pERK signaling in a dose-dependent manner with IC_{50} values of 0.59 μM and 0.63 ± 0.32 μM in NSCLC cells and NCI–H1975-OR cells, respectively.[1].

SHP2-IN-13 (0-30 μM; 24 hours) inhibited pERK levels and receptor tyrosine kinase (RTK)-driven cancer cell proliferation in NCI–H1975 cells, . And it also inhibits phosphorylated ERK (pERK) levels in receptor tyrosine kinase (RTK)-resistant NSCLC cells[1].

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

Western Blot Analysis[1]

Cell Line:	NSCLC cells or NCI–H1975-OR cells
Concentration:	0 μM, 0.01 μM, 0.04 μM, 0.1 μM, 0.4 μM, 1.1 μM, 3.3 μM, 10 μM, 30 μM
Incubation Time:	24 hours
Result:	Inhibited p-ERK expression in a dose-dependent manner.

In Vivo

In vivo pharmacokinetics studies, SHP2-IN-13 (compound 129) (IV/PO; 5mg/kg) demonstrates high clearance, a high volume of distribution (13.9 L/kg), a moderate half-life ($T_{1/2}$=5.31 h). Additionally, SHP2-IN-13 shows a higher oral bioavailability (F =55.07 ± 7.93%) than SHP099 (F =46%) and is suitable for further in vivo anti-tumor evaluation[1].

SHP2-IN-13 (oral gavage; 20 mg/kg; daily) exhibits an anti-leukaemic efficacy and causes significant reduction of leukemia burden. Additionally, it near completely eradicated human $CD45^+$ leukaemic cells in blood and spleen[1].

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Animal Model:	Murine NSG xenograft model inoculated with FLT3-ITD mutated MV-4-11-luciferase (MV-4-11-Luc) AML cells[1]
Dosage:	20 mg/kg
Administration:	Oral gavage; 20 mg/kg; daily

Result:	Exhibited an anti-tumour efficacy in AML model.

REFERENCES

[1]. Ruixiang Luo, et al. Discovery of a potent and selective allosteric inhibitor targeting the SHP2 tunnel site for RTK-driven cancer treatment. Eur J Med Chem. 2023 May 5;253:115305.

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