

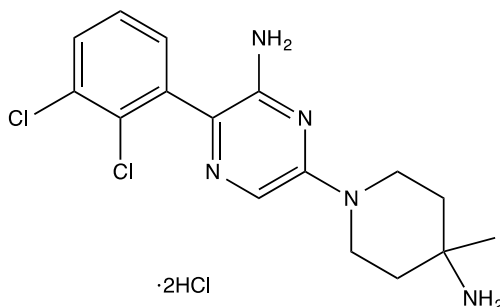
Catalog #10-4604

SHP099

CAS# 1801747-11-4

6-(4-Amino-4-methylpiperidin-1-yl)-3-(2,3-dichlorophenyl)pyrazin-2-amine dihydrochloride

Lot # FBA7052



SHP099 is a potent ($IC_{50} = 71$ nM) and selective allosteric inhibitor of SHP2. SHP2 is a non-receptor tyrosine phosphatase that regulates cell survival and proliferation through activating the RAS-ERK pathway. It also mediates programmed cell death 1 (PD-1) and T-lymphocyte attenuator (BTLA) immune checkpoint pathways. Treatment with SHP099, in combination with ceritinib, halts growth of ALK-inhibitor resistant non-small-cell lung cancer cells.³ Thus, reduction of SHP2 activity is a potential important cancer therapy target. It showed no activity against a panel of 21 other human phosphatases and 66 kinases. SHP099 has been recently shown to possess significant autophagy inhibition ($EC_{50} = 10.6$ μ M) activity in a SHP2-independent manner leading to significant anticancer therapeutic efficacies compared to SHP2 specific inhibitors.⁴

- 1) Fortanet *et al.* (2016), *Allosteric Inhibition of SHP2: Identification of a Potent, Selective, and Orally Efficacious Phosphatase Inhibitor*, J.Med.Chem. **59** 7773
- 2) Chen *et al.* (2016), *Allosteric inhibition of SHP2 phosphatase inhibits cancers driven by receptor tyrosine kinases*; Nature **535** 148
- 3) Dardaei *et al.* (2018), *SHP2 inhibition restores sensitivity in ALK-rearranged non-small-cell lung cancer resistant to ALK inhibitors*; Nat. Med. **24** 512
- 4) Miao *et al.* (2024), *Off-target autophagy inhibition by SHP2 allosteric inhibitors contributes to their antitumor activity in RAS-driven cancers*; J. Clin. Invest. **134** e177142

PHYSICAL DATA

Molecular Weight:	425.18
Molecular Formula:	C ₁₆ H ₁₉ Cl ₂ N ₅ ·2HCl
Purity:	>98% (HPLC)
	NMR: (Conforms)
Solubility:	DMSO (5 mg/mL) and water (>20 mg/mL)
Physical Description:	Yellow solid
Storage and Stability:	Store as supplied at -20°C for up to 1 year from the date of purchase. Solutions in DMSO or distilled water may be stored at -20°C for up to 3 months.

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Focus Biomolecules LLC 400 Davis Drive, Suite 600 Plymouth Meeting PA 19462

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