Product Data Sheet

Product Name: SHP099 HCl
Cat. No.: GC25930

Chemical Properties

Cas. No.	2200214-93-1		
Formula	C16H20Cl3N5	M.Wt	388.72
Solubility	DMSO: 78 mg/mL (200.66 mM);Water: 6 mg/mL (15.44 mM);Ethanol: Insoluble	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	SHP099 HCl		

Background

SHP099 is a highly potent, selective and orally bioavailable small-molecule SHP2 inhibitor with an IC50 value of 0.071 μM and shows no activity against SHP1.

SHP099 shows inhibition of cell proliferation (KYSE-520 model) with an IC50 of 1.4 μM. In both phosphatase and kinase panels, no biochemical inhibitory activity is evident, suggesting that the aminopyrazine series(SHP099) is quite selective for SHP2. Moreover, SHP099 shows high solubility (>0.5 mM in pH 6.8 buffer) and high permeability with no apparent efflux in Caco-2 cells[1]. SHP099 stabilizes SHP2 in an auto-inhibited conformation. SHP099 suppresses RAS-ERK signalling to inhibit the proliferation of receptor-tyrosine-kinase-driven human cancer cells in vitro. SHP099 only has modest activity against 5HT3 when profiled against a preclinical safety pharmacology panel representing 49 common adverse drug reaction targets. SHP099 shows no activity against SHP1, the closest homologue of SHP2 sharing 61% amino acid sequence identity, supporting its high degree of target selectivity. It inhibits p-ERK with an IC50 of ~0.25 μM in SHP2-dependent MDA-MB-468 and KYSE520 cells, but not in A2058 cells. No effect is observed on p-AKT levels across the same cells. SHP099 inhibits MAPK signalling and proliferation in RTK-dependent cells through direct on-target inhibition of SHP2[2].

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

SHP099 shows acceptable oral exposure (5 mg/kg PO, 565 μM/h) and bioavailability (46% F). SHP099 is a potent, selective, highly soluble, orally bioavailable, and efficacious SHP2 inhibitor exhibiting dose-dependent pathway inhibition and antitumor activity in xenograft models[1]. Orally administered SHP099 shows dose-dependent anti-tumour activity in the KYSE520 xenograft model and is well tolerated[2].

[1] Garcia Fortanet J, et al. J Med Chem. 2016, 59(17):7773-82. [2] Chen YN, et al. Nature. 2016, 535(7610):148-52.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA