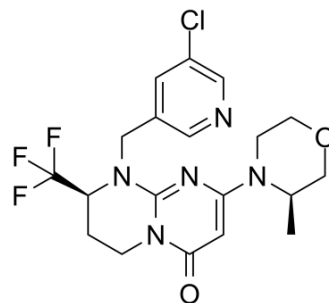


SAR405

Cat. No.:	HY-12481		
CAS No.:	1523406-39-4		
Molecular Formula:	C ₁₉ H ₂₁ ClF ₃ N ₅ O ₂		
Molecular Weight:	443.85		
Target:	PI3K; Autophagy		
Pathway:	PI3K/Akt/mTOR; Autophagy		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 27 mg/mL (60.83 mM)
 H₂O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.2530 mL	11.2651 mL	22.5301 mL
	5 mM	0.4506 mL	2.2530 mL	4.5060 mL
	10 mM	0.2253 mL	1.1265 mL	2.2530 mL

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

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (5.63 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.63 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.5 mg/mL (5.63 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
Solubility: ≥ 2.5 mg/mL (5.63 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SAR405 is a first-in-class, selective, and ATP-competitive PI3K class III (PIK3C3) isoform Vps34 inhibitor (IC₅₀=1.2 nM; K_D=1.5 nM). SAR405 inhibits autophagy induced either by starvation or by mTOR inhibition. Anticancer activity^{[1][2]}.

IC₅₀ & Target	Vps34 1.2 nM (IC ₅₀)	Vps34 1.5 nM (Kd)	Autophagy
In Vitro	<p>The activity of SAR405 is next evaluated on a dedicated Vps34 cellular assay using a GFP-FYVE-transfected HeLa cell line^[1]. SAR405 prevents autophagy and synergizes with mTOR inhibition in tumor cells. SAR405 prevents autophagosome formation with an IC₅₀ of 42 nM. Treatment of starved cells with SAR405 completely inhibits the conversion to LC3-II in a dose-dependent manner. The effect of SAR405 on autophagy is then investigated. The GFP-LC3 model is used for the HTS and confirmed its activity on starved cells (IC₅₀=419 nM). The conversion of LC3-I into LC3-II is also analyzed by western blotting on wild-type HeLa and H1299 cells^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>		

PROTOCOL

Kinase Assay ^[1]

KiNativ profiling is performed. Jurkat cell lysates are treated with 1 μM of SAR405. After 15-min incubation, the desthiobiotin-ATP-acylphosphate probe is added and incubated for 10 min. Samples are prepared for targeted MS analysis. Briefly, samples are prepared for trypsin digestion (denature and then reduce alkylate) and digested with trypsin, and desthiobiotinylated peptides are enriched on streptavidin resin. Enriched probe-labeled peptides are analyzed by LC tandem MS on a Thermo-LTQ ion trap mass spectrometer using proprietary data collection methodology. All quantification is performed by extracting characteristic fragment ion signals from targeted MS/MS spectra and comparing signals in control and treated samples^[1].

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

CUSTOMER VALIDATION

- Nat Genet. 2021 Apr;53(4):435-444.
- Mol Cell. 2021 Mar 18;81(6):1337-1354.e8.
- Nat Commun. 2021 Feb 26;12(1):1322.
- Nat Commun. 2020 Aug 13;11(1):4051.
- Nat Commun. 2018 Jan 18;9(1):291.

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REFERENCES

- [1]. Ronan B, et al. A highly potent and selective Vps34 inhibitor alters vesicle trafficking and autophagy. Nat Chem Biol. 2014 Dec;10(12):1013-9.
- [2]. Pasquier B. SAR405, a PIK3C3/Vps34 inhibitor that prevents autophagy and synergizes with MTOR inhibition in tumor cells. Autophagy. 2015 Apr 3;11(4):725-6.

Caution: Product has not been fully validated for medical applications. For research use only.

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