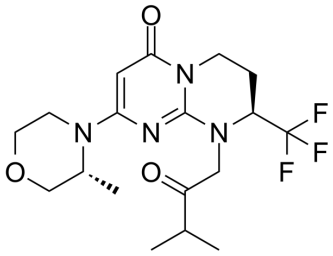
Vps34-IN-2

Cat. No.:	HY-12473
CAS No.:	1523404-29-6
Molecular Formula:	$C_{18}H_{25}F_3N_4O_3$
Molecular Weight:	402.41
Target:	PI3K; SARS-CoV
Pathway:	PI3K/Akt/mTOR; Anti-infection
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 50 mg/mL (124.25 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.4850 mL	12.4251 mL	24.8503 mL
5 mM	0.4970 mL	2.4850 mL	4.9701 mL
10 mM	0.2485 mL	1.2425 mL	2.4850 mL

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

In Vivo

1. Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.21 mM); Clear solution
2. Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.21 mM); Clear solution
3. Add each solvent one by one: 10% EtOH >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.21 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vps34-IN-2 is a novel, potent and selective inhibitor of Vps34 with IC_{50}s of 2 and 82 nM on the Vps34 enzymatic assay and the GFP-FYVE cellular assay, respectively[1]. Vps34-IN-2 shows antiviral activity against SARS-CoV-2 (IC_{50} of 3.1 μM), HCoV-229E (IC_{50} of 0.7 μM) and HCoV-OC43[2].

IC_{50} & Target			
	Vps34 2 nM (IC_{50})	SARS-CoV-2 3.1 μM (IC_{50})	HCoV-229E 0.7 μM (IC_{50})

In Vitro	Vps34-IN-2 (Compound 31) displays IC_{50}s of 2 and 82 nM on the Vps34 enzymatic assay and the GFP-FYVE cellular assay, respectively. Vps34-IN-2 exhibits selectivity against mTOR (IC_{50}>10 μM) and class I PI3Ks (IC_{50} values of 2.7, 4.5, 2.5, and >10 μM on PI3K α, β, δ, γ isoforms, respectively)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	After administration by the intravenous (iv) route, Vps34-IN-2 (Compound 31) concentrations are quantifiable up to 6, 8, and 24 h (last sampling time) depending on animals. After oral administration (po), Vps34-IN-2 is rapidly absorbed with maximal plasma concentrations observed at 0.5 h and a bioavailability of 85%. Slight rebounds of concentrations are observed at 4 and 8 h after oral dosing with no obvious explanation. After iv injection of Vps34-IN-2 at 3 mg/kg, plasma clearance is found moderate (i.e., 2.3 L/h/kg), corresponding to 44% of hepatic blood flow in this species, volume of distribution at steady state is moderate, and terminal elimination half-life is short[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	Cells are cultured in RPMI-1640 medium with 10% fetal bovine serum. Cells are lysed by sonication in a detergent containing lysis buffer and cleared by centrifugation, and the resulting supernatant is collected for compound treatment. Final protein concentration of lysates is 4 mg/mL. An amount of 5 μL of Vps34-IN-2 (Compound 31) is added from 100× stock solutions in DMSO to 445 μL of lysate in duplicate. An amount of 5 μL of DMSO is added to 445 μL of lysate in quadruplicate for controls. After 15 min incubation, 5 μL of a 100× aqueous solution of the ATP probe I is added to each sample (final concentration of ATP probe I is 0.5 μM). After 5 min, 50 μL of a 10× aqueous solution of the ATP probe II is added to each sample (final concentration of ATP probe II is 20 μM). All samples are then incubated for an additional 10 min[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	For PK/PD studies, 3×10^6 H1299-GFP-FYVE tumor cells with 50% Matrigel are subcutaneously injected on the dorsal side of SCID mice, one tumor per mouse. When xenografted tumors reach a range of ~200 to 400 mm^3, mice are treated with vehicle (98% PEG200/2% PS80) or a single dose of Vps34-IN-2 (compound 31) at 100 and 50 mg/kg via oral gavage. Three mice treated with vehicle alone and three mice treated with Vps34-IN-2 are sacrificed at each time point; tumor tissues are harvested for immunohistochemistry (IHC) analysis and plasma samples are collected to determine the concentration of Vps34-IN-2[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.
- J Virol. 2021 Sep 22;JVI0153721.

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REFERENCES

[1]. Pasquier B, et al. Discovery of (2S)-8-[(3R)-3-methylmorpholin-4-yl]-1-(3-methyl-2-oxobutyl)-2-(trifluoromethyl)-3,4-dihydro-2H-pyrimido[1,2-a]pyrimidin-6-one: a novel potent and selective inhibitor of Vps34 for the treatment of solid tumors. J Med Chem. 2015 Jan 8;58(1):376-400.

[2]. Jim Baggen, et al. Genome-wide CRISPR screening identifies TMEM106B as a proviral host factor for SARS-CoV-2. Nat Genet. 2021 Mar 8.

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

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