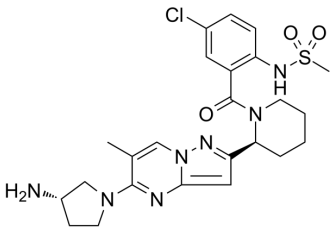
Presatovir

Cat. No.:	HY-16727
CAS No.:	1353625-73-6
Molecular Formula:	$C_{24}H_{30}ClN_7O_3S$
Molecular Weight:	532.06
Target:	RSV
Pathway:	Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 6 mg/mL (11.28 mM; Need ultrasonic and warming)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8795 mL	9.3974 mL	18.7949 mL
5 mM	0.3759 mL	1.8795 mL	3.7590 mL
10 mM	0.1879 mL	0.9397 mL	1.8795 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.6 mg/mL (1.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.6 mg/mL (1.13 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.6 mg/mL (1.13 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 0.48 mg/mL (0.90 mM); Clear solution
5. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.48 mg/mL (0.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Presatovir (GS-5806) is an orally bioavailable RSV fusion inhibitor with a mean EC_{50} value of 0.43 nM[1].

IC_{50} & Target	EC50: 0.43 nM (RSV)[1]
In Vitro	Presatovir is a novel, orally bioavailable RSV fusion inhibitor discovered following a lead optimization campaign on a hit originated from a phenotypic RSV antiviral high-throughput screen. Presatovir exhibits potent activity against a wide range of RSV A and B clinical isolates with a mean EC_{50} value of 0.43 nM[1]. GS-5806 inhibits pre to post triggered conformational changes of RSV F protein, suggesting a possible mechanism for antiviral activity[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Presatovir demonstrates dose-dependent (0-30 mg/kg) antiviral efficacy in a cotton rat model of RSV infection. Oral bioavailability in preclinical species ranges from 46 to 100%, with penetration of the compound into the lung tissue demonstrated in Sprague-Dawley rats. Multidose oral treatment of Presatovir appears safe in adults, and in healthy human volunteers experimentally infected with RSV, a potent antiviral effect and reduction in disease severity is observed in the high dose group. A group treated with a lower dose of Presatovir allows for a PK-PD relationship to be established to help guide future dose selections[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	GS-5806 are diluted in 100% DMSO. To conduct the cytopathic antiviral assay, 0.4 µL of 100×concentrated 3-fold serially diluted drug is added to 20 µL of cell culture medium in a 384-well plate. HEp-2 cells are then suspended in MEM plus 10% FBS at a density of 1×10^5 cells/mL, are infected in bulk with RSV A2 at a titer of approximately $1\times10^{4.5}$ tissue culture infectious doses/mL. Immediately following infection, 20 µL of RSV-infected cells are added to each well. The cells are then cultured for 4 days at 37 °C. Following this incubation the cells are allowed to equilibrate to 25°C. The RSV-induced cytopathic effect is determined by adding 40 µL of Cell-Titer Glo viability reagent. Following a 10 min incubation at 25 °C, cell viability is determined[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- J Enzyme Inhib Med Chem. 2022 Dec;37(1):2598-2604.
- J Virol. 2021 Aug 11;JVI0120521.
- J Antimicrob Chemother. 2018 Jul 1;73(7):1823-1829.

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REFERENCES

[1]. Mackman RL, et al. Discovery of an oral respiratory syncytial virus (RSV) fusion inhibitor (GS-5806) and clinical proof of concept in a human RSV challenge study. J Med Chem. 2015 Feb 26;58(4):1630-1643.

[2]. Samuel D, et al. GS-5806 inhibits pre- to postfusion conformational changes of the respiratory syncytial virus fusion protein. Antimicrob Agents Chemother. 2015 Nov;59(11):7109-12.

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

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