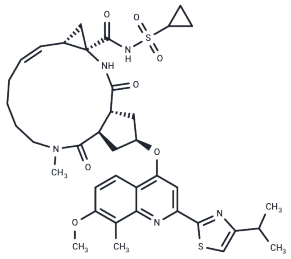
Data Sheet (Cat.No.T4686)

TargetMol

Simeprevir

Chemical Properties



CAS No. : 923604-59-5

Formula: C38H47N5O7S2

Molecular Weight: 749.94

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Simeprevir (TMC435) is a potent HCV NS3/4A protease inhibitor, and inhibits HCV replication with EC50 of 8 nM.
Targets(IC50)	HCV Protease,SARS-CoV
In vitro	In Huh7-Luc cells, antiviral activity of simeprevir (Simeprevir) is dose dependent, and the EC50 and EC90 values determined for Simeprevir are 8 nM and 24 nM, respectively. Inhibition of Simeprevir on NS3/4A protease is time dependent, and the overall Kis are estimated to be 0.5 nM for genotype 1a and 0.4 nM for genotype 1b, respectively. Simeprevir is a potent inhibitor of HCV NS3/4A protease (Ki=0.36 nM) and viral replication (replicon EC50=7.8 nM).
In vivo	In rats, TMC435350 (40 mg/kg, p.o.) is extensively distributed to the liver and intestinal tract (tissue/plasma area under the concentration-time curve ratios of >35), and the absolute bioavailability is 44%.
Kinase Assay	In vitro inhibition of NS3/4A activity is determined using a fluorescence resonance energy transfer cleavage assay with the RetS1 peptide substrate, derived from the genotype 1a NS4A-4B junction, and bacterially expressed full-length NS3 protease domain, supplemented with an NS4A peptide. Briefly, NS3/4A is preincubated in the presence of TMC435350 for 10 min, and then the RetS1 substrate is added and fluorescence is continuously measured for 20 min (excitation, 355 nm; emission, 500 nm). Cleavage of the substrate is expressed as a percentage of the cleavage seen with the vehicle control.
Cell Research	Huh7-Luc cells are seeded at a density of 2,500 cells/well in a 384-well plate in Dulbecco's modified Eagle's medium plus 10% fetal calf serum and incubated with a range of concentrations of serially diluted simeprevir, in a final DMSO concentration of 0.5% in the absence of G418. After 72 h of incubation, Steady Lite reagent is added in a 1:1 ratio to the medium, and luciferase signal is measured using a ViewLux reader.
Animal Research	Twenty-four male specific-pathogen-free Sprague-Dawley rats, weighing between 200 and 300 g at the time of dosing, are divided into eight groups of three rats each. Seven groups are dosed orally (p.o.) by gastric intubation of a vitamin E acetate-d-α-tocopheryl polyethylene glycol 1000 succinate-polyethylene glycol 400 solution of Simeprevir (TMC435350) at 2 mL/kg body weight to provide a dose of 40 mg/kg. One group is dosed intravenously (i.v.) by slow bolus injection in a tail vein of a 20% 2-hydroxypropyl-β-cyclodextrin formulation of TMC435350 (containing TMC435350, 100

	mg/mL 2-hydroxypropyl-β-cyclodextrin, 0.1 N NaOH to pH 8.0±0.1, and mannitol-and pyrogen-free water) at 2 mL/kg body weight to provide a dose of 4 mg/kg. Water and food are available ad libitum during the study.

Solubility Information

Solubility	DMSO: 55 mg/mL (73.34 mM),Sonication is recommended. H2O: Insoluble, (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.3334 mL	6.6672 mL	13.3344 mL
5 mM	0.2667 mL	1.3334 mL	2.6669 mL
10 mM	0.1333 mL	0.6667 mL	1.3334 mL
50 mM	0.0267 mL	0.1333 mL	0.2667 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Lin TI, et al. In vitro activity and preclinical profile of TMC435350, a potent hepatitis C virus protease inhibitor. Antimicrob Agents Chemother. 2009 Apr;53(4):1377-85. Epub 2009 Jan 26.

Sinokki A, Miinalainen A, Kiander W, et al.PREINCUBATION-DEPENDENT INHIBITION OF ORGANIC ANION TRANSPORTING POLYPEPTIDE 2B1.European Journal of Pharmaceutical Sciences.2024: 106852.

Raboisson P, et al. Structure-activity relationship study on a novel series of cyclopentane-containing macrocyclic inhibitors of the hepatitis C virus NS3/4A protease leading to the discovery of TMC435350. Bioorg Med Chem Lett. 2008 Sep 1;18(17):4853-8.

Zhang X, et al. Discovery and evolution of aloperine derivatives as a new family of HCV inhibitors with novel mechanism. Eur J Med Chem. 2018 Jan 1;143:1053-1065.