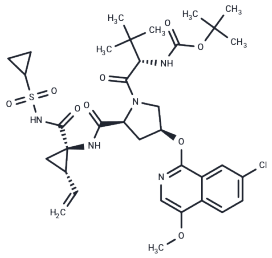
Data Sheet (Cat.No.T4474)

TargetMol

Asunaprevir

Chemical Properties



CAS No. : 630420-16-5

Formula: C35H46ClN5O9S

Molecular Weight: 748.29

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Asunaprevir (BMS-650032) is an effective hepatitis C virus (HCV) NS3 protease inhibitor.
Targets(IC50)	HCV Protease,SARS-CoV
In vitro	Asunaprevir inhibits the NS3 proteolytic activity of genotype 1a (H77 strain) and genotype 1b (J4L6S strain), with IC50s of 0.7 and 0.3 nM, respectively. The EC50s of ASV against replicons encoding the NS3 protease domains representing genotypes 1a, 1b, and 4a, range from 1.2 to 4.0 nM[2]. Replicon cells are maintained under selective pressure with asunaprevir at concentrations of 10 and 30 times the EC50 values (50 or 150 nM final concentrations, respectively). For genotype 1b resistance selection, replicon cells are maintained in the presence of asunaprevir at 10 or 30 times the EC50 values (30 or 90 nM final concentrations, respectively)[3]. Asunaprevir, administered at single or multiple doses of 200 to 600 mg twice daily, is generally well tolerated, achieving rapid and substantial decreases in HCV RNA levels in subjects chronically infected with genotype 1 HCV[4].
In vivo	Asunaprevir, administered orally at doses ranging from 3-15 mg/kg, exhibits a hepatotropic disposition, evidenced by liver-to-plasma ratios spanning from 40 to 359 across different animal species. Twenty-four hours after administration, liver exposure levels in all evaluated species were at least 110 times greater than the inhibitor EC50 noted against HCV genotype-1 replicons[2].
Cell Research	Cytotoxicity is determined by incubating cells (3,000 to 10,000 cells/well) with serially diluted test compounds or DMSO for 5 days (MT-2 cells) or 4 days (all other cell types). Cell viability is quantitated using an MTS assay for MT-2 or a Cell-Titer Blue reagent assay for HEK-293, HuH-7, HepG2, and MRC5 cells, and 50% cytotoxic concentrations (CC50s) are calculated.
Animal Research	Mice (n=9 per group; overnight fast) receive Asunaprevir (ASV) by oral gavage (5 mg/kg; a vehicle of PEG-400-ethanol, 9:1). Blood samples (-0.2 mL) are obtained by retro-orbital bleeding at 0.25, 0.5, 1, 3, 6, 8, and 24 h after dosing. Within each group, three animals are bled at 0.25, 3, and 24 h, three at 0.5 and 6 h, and three at 1 and 8 h, resulting in a composite pharmacokinetic profile. Livers and brains are also removed from mice at the terminal sampling points. Rats (n=3 per group; overnight fast) receive ASV (amorphous free acid) by oral gavage (3, 5, 10, and 15 mg/kg) in PEG-400-ethanol (9:1). Serial blood samples (-0.3 mL) are obtained from the jugular vein predosing (0 h)

Animal Research	and at 0.25, 0.5, 0.75, 1, 2, 4, 6, 8, 24, and 48 h post dosing. To assess tissue exposure, rats are orally administered ASV (5 or 15 mg/kg, same vehicle as above), and blood, liver, and heart samples from two rats/group are obtained at 0.17, 0.5, 1, 2, 4, 6, 8, 24, 48, and 72 h after dosing.

Solubility Information

Solubility	H2O: Insoluble, Ethanol: 20 mg/mL (26.73 mM),Sonication is recommended. DMSO: 250 mg/mL (334.1 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Corn oil: 10 mg/mL (13.36 mM),Solution. 10% DMSO+90% Saline: < 10 mg/mL (13.36 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+90% (20% SBE-β-CD in Saline): < 10 mg/mL (13.36 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: < 10 mg/mL (13.36 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.3364 mL	6.6819 mL	13.3638 mL
5 mM	0.2673 mL	1.3364 mL	2.6728 mL
10 mM	0.1336 mL	0.6682 mL	1.3364 mL
50 mM	0.0267 mL	0.1336 mL	0.2673 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Pelosi LA, et al. Effect on HCV Replication by Combinations of Direct Acting Antivirals Including NS5A Inhibitor Daclatasvir. Antimicrob Agents Chemother. 2012 Jul 30.
McPhee F, et al. Preclinical Profile and Characterization of the Hepatitis C Virus NS3 Protease Inhibitor Asunaprevir (BMS-650032). Antimicrob Agents Chemother. 2012 Aug 6.
McPhee F, et al. Resistance analysis of the hepatitis C virus NS3 protease inhibitor asunaprevir. Antimicrob Agents Chemother. 2012 Jul;56(7):3670-81.
Pasquinelli C, et al. Single- and multiple-ascending-dose studies of the NS3 protease inhibitor asunaprevir in subjects with or without chronic hepatitis C. Antimicrob Agents Chemother. 2012 Apr;56(4):1838-44.

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