Datasheet

Telaprevir

Product Name	Telaprevir (VX-950)
Catalogue Number	BSV-S1538
Chemical Formula	$C_{36}H_{53}N_7O_6$
Function	HCV protease inhibitor
CAS No.:	402957-28-2

Description:

Telaprevir (VX-950) is an **HCV NS3-4A serine protease** inhibitor with **IC50** of 0.35 μM.

Product Details:

Target: HCV NS3-4A serine protease [1]

Chemical name: (1S,3aR,6aS)-2-((S)-2-((S)-2-cyclohexyl-2-(pyrazine-2-carboxamido)acetamido)-3,3-dimethylbutanoyl)-N-((S)-1-(cyclopropylamino)-1,2-dioxohexan-3-yl)-octahydrocyclopenta[c]pyrrole-1-carboxamide

Formula: $C_{36}H_{53}N_7O_6$

Molecular weight: 679.85

Purity: 98.70 % (HPLC)

Solubility: 136 mg/mL (DMSO)

Storage: 3 years -20°C powder, 2 years -80°C in solvent

Regulatory/ Restrictions: For laboratory use only.

Preparing stock solutions:

Concentration/ Mass	1 mg	5 mg	10 mg
1 mM	1.4709 mL	7.3546 mL	14.7091 mL
5 mM	0.2942 mL	1.4709 mL	2.9418 mL
10 mM	0.1471 mL	0.7355 mL	1.4709 mL
50 mM	0.0294 mL	0.1471 mL	0.2942 mL

Biological activity:

In vitro:
Telaprevir inhibits the hepatitis C virus NS3-4A serine protease, leading to the block of viral polyprotein processing and subsequently decrease of viral RNA replication, total HCV RNA levels and protein levels in the Con1 (genotype 1b) subgenomic HCV replicon cells in a time- and dose-dependent manner. Telaprevir displays a significant time-dependent increase in inhibitory effect on the replication of HCV RNA with IC50 values of 0.574 μM, 0.488 μM, 0.210 μM and 0.139 μM for 24, 48, 72 and 120 hours incubation, respectively. Telaprevir displays an average IC50 of 0.354 μM and an average IC90 of 0.830 μM, respectively, from three independent experiments using the 48 hours incubation. Telaprevir has no significant cytotoxicity to HCV replicon cells, parental Huh-7 and HepG2 cells after 48 hours incubation. Telaprevir (17.5 μM) completely eradicates HCV RNA from replicon cells after 13 days incubation without rebound after Telaprevir is withdrawn. Telaprevir displays an additive to moderate synergistic effect on reduction of HCV RNA replication and suppression of resistance mutations without significant increase in cytotoxicity when in combination with IFN-α, compared to treatment with each agent alone. [1]

In vivo:
Oral administration of Telaprevir reduces HCV protease-dependent cleavage and subsequent secretion of SEAP from the liver into the blood in the mice model to 18.7% and 18.4% at dosage of 10 and 25 mg/kg, respectively. [2] Administration of Telaprevir at 200 mg/kg for 1 week results in a 1.9 log reduction of HCV RNA in genotype 1b HCV-infected human hepatocyte chimeric mice, and when treatment in combination with MK-0608 (50 mg/kg) for 4 weeks, viruses are eliminated from mice. [3]

Telaprevir is a covalent, reversible inhibitor of the NS3-4A protease (unlike BILN 2061which is a noncovalent inhibitor), with a slow-binding and slow-dissociation mechanism.

Protocol *(Only for Reference)*

Kinase Assay: [1]	
Determination of anti-HCV activity	Stable Huh-7 cells containing the self-replicating, subgenomic HCV replicon, which is identical in sequence to the I_{377}neo/NS3-3'/wt replicon are used for anti-HCV assays. Replicon cells are incubated at 37 °C for the indicated period of time with Telaprevir serially diluted in DMEM plus 2% FBS and 0.5% dimethyl sulfoxide (DMSO). Total cellular RNA is extracted using an RNeasy-96 kit, and the copy number of HCV RNA is determined using a quantitative RTPCR (QRT-PCR) assay for the assessment of 50% inhibitory concentration (IC50)
Cell Assay: [1]	
Cell lines	Huh-7, HepG2, and peripheral blood mononuclear cells (PBMC)
Concentrations	Dissolved in DMSO, final concentration ~1 mM
Incubation Time	48 hours
Method	Cells are incubated with various concentrations of Telaprevir for 48 hours. Cell viability is determined by using a tetrazolium (MTS)-based cell viability assay.
Animal Study: [2]	
Animal Models	SCID mice injected with recombinant adenovirus (Ad-WT-HCVpro-SEAP or Ad-MT-HCVpro-SEAP)
Dosages	~300 mg/kg
Administration	Oral gavage

References:

[1] Lin K, et al. Antimicrob Agents Chemother, 2006, 50(5), 1813-1822.
[2] Perni RB, et al. Antimicrob Agents Chemother, 2006, 50(3), 899-909.
[3] Ohara E, et al. J Hepatol, 2011, 54(5), 872-878.