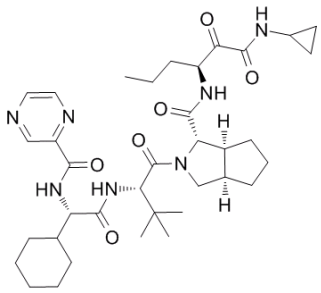
Data Sheet

MSDS Reviewed, no changes.
Extended to 12-Jan-2024
Noted: 12-Jan-2021 BW

Product Name:	Telaprevir
Cat. No.:	CS-0285
CAS No.:	402957-28-2
Molecular Formula:	$C_{36}H_{53}N_7O_6$
Molecular Weight:	679.85
Target:	HCV; HCV Protease
Pathway:	Anti–infection; Metabolic Enzyme/Protease
Solubility:	10 mM in DMSO



BIOLOGICAL ACTIVITY:

Telaprevir is a highly selective, reversible, and potent peptidomimetic inhibitor of the **HCV NS3–4A protease**, the steady–state inhibitory constant (**Ki**) of Telaprevir is 7 nM against a genotype 1 (H strain) NS3 protease domain plus a NS4A cofactor peptide. IC50 & Target: Ki: 7 nM (genotype 1 HCV NS3–4A protease)[1]

In Vitro: Telaprevir (VX–950) is a covalent, reversible inhibitor of the NS3–4A protease with a slow–binding and slow–dissociation mechanism. Telaprevir exhibits significantly different kinetics in enzyme inhibition, which is most clearly exemplified by a very long half–life (58 min) of the bound enzyme–inhibitor complex. Telaprevir is additive to moderately synergistic with IFN–α in inhibiting HCV replication and in suppressing the emergence of resistance in replicon cells. Telaprevir reduces HCV RNA levels in a time– and dose–dependent manner. The IC_{50}s following a 24, 48, 72, and 120 h incubation with Telaprevir are determined to be 0.574, 0.488, 0.21, and 0.139 μM, respectively, indicating an increase in inhibitory effects with time. Following three independent experiments using the 48 h incubation in the presence of 2% FBS, the average IC_{50} of Telaprevir is determined to be 0.354 ± 0.035 μM, and the average IC_{90} is 0.830 ± 0.190 μM[1]. Telaprevir (VX–950) is a potent, selective, peptidomimetic inhibitor of the hepatitis C virus (HCV) NS3–4A serine protease, and Telaprevir demonstrates excellent antiviral activity both in genotype 1b HCV replicon cells (IC_{50}=354 nM) and in human fetal hepatocytes infected with genotype 1a HCV–positive patient sera (IC_{50}=280 nM)[2].

In Vivo: There is an ~5–fold reduction of serum SEAP activity in mice dosed with Telaprevir (VX–950) at either 10 or 25 mg/kg, which has an average value (±SEM) of 18.7±8.3% or 18.4±5.4%, respectively, compare to those administered vehicle (100±28%). These data demonstrates that Telaprevir is able to inhibit the HCV NS3–4A serine protease activity in mouse liver and block cleavage and subsequent secretion of SEAP into blood circulation in these mice[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Telaprevir (VX–950) is dissolved in DMSO and stored, and then diluted with appropriate media before use[1].[1]Determination of IC_{50}, IC_{90}, CC_{50} of Telaprevir (VX–950) or IFN–α in HCV replicon cells is performed. Briefly, 1×10^4 replicon cells per well are plated in 96–well plates. On the following day, replicon cells is incubated at 37°C for the indicated period of time with antiviral agents serially diluted in DMEM plus 2% FBS and 0.5% DMSO. Total cellular RNA is extracted using an RNeasy–96 kit, and the copy number of HCV RNA is determined using a quantitative RT–PCR (QRT–PCR) assay. Each datum point represents the average of five replicates in cell culture. The cytotoxicity of Telaprevir is measured under the same experimental settings using a tetrazolium (MTS)–based cell viability assay. For the cytotoxicity assay with human hepatocyte cell lines, 1×10^4 parental Huh–7 cells per well or 4×10^4 HepG2 cells per well are used. To determine cytotoxicity of Telaprevir against resting PBMC, 1×10^5 cells per well are incubated with Telaprevir in RPMI–1640 medium (no serum) for 48 h, and the cell viability is determined by the MTS–based assay.

To determine cytotoxicity of VX–950 against proliferating PBMC, 1×10^5 cells per well in RPMI–1640 medium are added to a 96–well plate, which is precoated with anti–human CD3 antibody. The cells are incubated with Telaprevir and anti–human CD28 antibody for 72 h at 37°C, and the cell growth is determined by [^{3}H]thymidine update between the 48th and 72nd h[1].

Animal Administration: Telaprevir (VX–950) is prepared in 15% ethanol, 10% dimethyl isosorbide, 35% polyethylene glycol 400, and 40% D5W (5% dextrose in water) (intravenous bolus)[2].

Telaprevir (VX–950) is formulated in polyvinylpyrrolidone (PVP) K–30 plus 2% sodium lauryl sulfate (orally)[2].[2]Mice[2]

Five groups of 6–week–old SCID mice (6 animals per group) are injected with 10^9 IFU per mouse of recombinant adenovirus Ad–WT–HCVpro–SEAP through the tail vein. Each group of mice is given two oral administrations of Telaprevir (VX–950) at one of the following doses: 10, 25, 75, 150, or 300 mg/kg. The first Telaprevir dose is given 2 h before the adenovirus injection, and the second dose is given 10 h after injection. An additional group of 10 mice is given vehicle alone. Serum samples are collected 24 h postinjection, and the SEAP activity in each Telaprevir–dosed group is compared to that of the vehicle group. Rat and Dog[2] The intravenous and oral pharmacokinetics of Telaprevir (VX–950) are evaluated in rats and dogs. A group of 3 male Sprague–Dawley rats weighing 250 to 300 g is administered an intravenous bolus dose of 0.95 mg/kg Telaprevir. Serial blood samples are collected in heparinized tubes before dosing and at 0.083, 0.167, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, and 8 h after dose administration. A group of 3 male beagle dogs (8 to 12 kg) is administered an intravenous bolus dose of 3.5 mg/kg Telaprevir in 10% ethanol, 40% polyethylene glycol 400, and 50% D5W. Serial blood samples are collected in heparinized tubes before dosing and at 0.083, 0.167, 0.25, 0.5, 1, 1.5, 2, 4, 6, 8, 12, and 24 h after dose administration. For oral studies in rats and dogs, Telaprevir is formulated in polyvinylpyrrolidone (PVP) K–30 plus 2% sodium lauryl sulfate and then dosed as an oral gavage. A group of 3 male Sprague–Dawley rats (250 to 300 g) is dosed orally with 40 mg/kg VX–950, and a group of 4 male beagle dogs (10.9 to 12.0 kg) is administered an oral dose of 9.6 mg/kg VX–950. In both oral studies, blood samples are taken before dosing and at 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 h after dose administration. In both intravenous and oral studies, plasma samples are obtained by centrifugation and stored at -70°C

References:

[1]. Lin K, et al. VX–950, a novel hepatitis C virus (HCV) NS3–4A protease inhibitor, exhibits potent antiviral activities in HCv replicon cells. Antimicrob Agents Chemother. 2006 May;50(5):1813–22.

[2]. Perni RB, et al. Preclinical profile of VX–950, a potent, selective, and orally bioavailable inhibitor of hepatitis C virus NS3–4A serine protease. Antimicrob Agents Chemother. 2006 Mar;50(3):899–909.

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA

Certificate of Analysis

Product Name:	Telaprevir
Cat. No.:	CS-0285
CAS No.:	402957-28-2
Batch No.:	06342
Chemical Name:	Cyclopenta[c]pyrrole-1-carboxamide, (2S)-2-cyclohexyl-N-(2-pyrazinylcarbonyl)glycyl-3-methyl-L-valyl-N-[(1S)-1-[2-(cyclopropylamino)-2-oxoacetyl]butyl]octahydro-, (1S,3aR,6aS)-

PHYSICAL AND CHEMICAL PROPERTIES

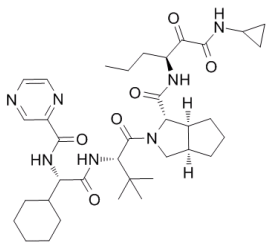
Molecular Formula: $C_{36}H_{53}N_7O_6$

Molecular Weight: 679.85

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month

Chemical Structure:



ANALYTICAL DATA

Appearance:	White to off-white (Solid)
^{1}H NMR Spectrum:	Consistent with structure
HPLC:	Consistent with structure
Purity (HPLC):	99.65%
Conclusion:	The product has been tested and complies with the given specifications.

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

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Safety Data Sheet

Revision Date: Nov.-08-2017
Print Date: Nov.-08-2017

1. PRODUCT AND COMPANY IDENTIFICATION

1.1 Product identifier

Product name : Telaprevir

Catalog No. : CS-0285

CAS No. : 402957-28-2

1.2 Relevant identified uses of the substance or mixture and uses advised against

Identified uses : Laboratory chemicals, manufacture of substances.

1.3 Details of the supplier of the safety data sheet

Company: ChemScene LLC

Tel: 732-484-9848

Fax: 888-484-5008

E-mail: sales@chemscene.com

1.4 Emergency telephone number

Emergency Phone #: 732-484-9848

2. HAZARDS IDENTIFICATION

2.1 Classification of the substance or mixture

Not a hazardous substance or mixture.

2.2 GHS Label elements, including precautionary statements

Not a hazardous substance or mixture.

2.3 Other hazards

None.

3. COMPOSITION/INFORMATION ON INGREDIENTS

3.1 Substances

Synonyms: VX–950; VX950; VX 950

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

Molecular Weight: 679.85

CAS No. : 402957-28-2

4. FIRST AID MEASURES

4.1 Description of first aid measures

Eye contact

Remove any contact lenses, locate eye-wash station, and flush eyes immediately with large amounts of water. Separate eyelids with fingers to ensure adequate flushing. Promptly call a physician.

Skin contact

Rinse skin thoroughly with large amounts of water. Remove contaminated clothing and shoes and call a physician.

Inhalation

Immediately relocate self or casualty to fresh air. If breathing is difficult, give cardiopulmonary resuscitation (CPR). Avoid mouth-to-mouth resuscitation.

Ingestion

Wash out mouth with water; Do NOT induce vomiting; call a physician.

4.2 Most important symptoms and effects, both acute and delayed

The most important known symptoms and effects are described in the labelling (see section 2.2).

4.3 Indication of any immediate medical attention and special treatment needed

Treat symptomatically.

5. FIRE FIGHTING MEASURES

5.1 Extinguishing media

Suitable extinguishing media

Use water spray, dry chemical, foam, and carbon dioxide fire extinguisher.

5.2 Special hazards arising from the substance or mixture

During combustion, may emit irritant fumes.

5.3 Advice for firefighters

Wear self-contained breathing apparatus and protective clothing.

6. ACCIDENTAL RELEASE MEASURES

6.1 Personal precautions, protective equipment and emergency procedures

Use full personal protective equipment. Avoid breathing vapors, mist, dust or gas. Ensure adequate ventilation. Evacuate personnel to safe areas.

Refer to protective measures listed in sections 8.

6.2 Environmental precautions

Try to prevent further leakage or spillage. Keep the product away from drains or water courses.

6.3 Methods and materials for containment and cleaning up

Absorb solutions with finely-powdered liquid-binding material (diatomite, universal binders); Decontaminate surfaces and equipment by scrubbing with alcohol; Dispose of contaminated material according to Section 13.

7. HANDLING AND STORAGE

7.1 Precautions for safe handling

Avoid inhalation, contact with eyes and skin. Avoid dust and aerosol formation. Use only in areas with appropriate exhaust ventilation.

7.2 Conditions for safe storage, including any incompatibilities

Keep container tightly sealed in cool, well-ventilated area. Keep away from direct sunlight and sources of ignition.

Recommended storage temperature:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month

Shipping at room temperature if less than 2 weeks.

7.3 Specific end use(s)

No data available.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1 Control parameters

Components with workplace control parameters

This product contains no substances with occupational exposure limit values.

8.2 Exposure controls

Engineering controls

Ensure adequate ventilation. Provide accessible safety shower and eye wash station.

Personal protective equipment

Eye protection	Safety goggles with side-shields.
Hand protection	Protective gloves.
Skin and body protection	Impervious clothing.
Respiratory protection	Suitable respirator.
Environmental exposure controls	Keep the product away from drains, water courses or the soil. Clean spillages in a safe way as soon as possible.

9. PHYSICAL AND CHEMICAL PROPERTIES

9.1 Information on basic physical and chemical properties

Appearance	White to off-white (Solid)
Odor	No data available
Odor threshold	No data available
pH	No data available
Melting/freezing point	No data available
Boiling point/range	No data available
Flash point	No data available
Evaporation rate	No data available
Flammability (solid, gas)	No data available
Upper/lower flammability or explosive limits	No data available
Vapor pressure	No data available
Vapor density	No data available
Relative density	No data available
Water Solubility	No data available
Partition coefficient	No data available
Auto-ignition temperature	No data available
Decomposition temperature	No data available
Viscosity	No data available
Explosive properties	No data available
Oxidizing properties	No data available

9.2 Other safety information

No data available.

10. STABILITY AND REACTIVITY

10.1 Reactivity

No data available.

10.2 Chemical stability

Stable under recommended storage conditions.

10.3 Possibility of hazardous reactions

No data available.

10.4 Conditions to avoid

No data available.

10.5 Incompatible materials

Strong acids/alkalis, strong oxidising/reducing agents.

10.6 Hazardous decomposition products

Under fire conditions, may decompose and emit toxic fumes.

Other decomposition products - no data available.

11.TOXICOLOGICAL INFORMATION

11.1 Information on toxicological effects

Acute toxicity

Classified based on available data. For more details, see section 2

Skin corrosion/irritation

Classified based on available data. For more details, see section 2

Serious eye damage/irritation

Classified based on available data. For more details, see section 2

Respiratory or skin sensitization

Classified based on available data. For more details, see section 2

Germ cell mutagenicity

Classified based on available data. For more details, see section 2

Carcinogenicity

IARC: No component of this product present at a level equal to or greater than 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

ACGIH: No component of this product present at a level equal to or greater than 0.1% is identified as a potential or confirmed carcinogen by ACGIH.

NTP: No component of this product present at a level equal to or greater than 0.1% is identified as a anticipated or confirmed carcinogen by NTP.

OSHA: No component of this product present at a level equal to or greater than 0.1% is identified as a potential or confirmed carcinogen by OSHA.

Reproductive toxicity

Classified based on available data. For more details, see section 2

Specific target organ toxicity - single exposure

Classified based on available data. For more details, see section 2

Specific target organ toxicity - repeated exposure

Classified based on available data. For more details, see section 2

Aspiration hazard

Classified based on available data. For more details, see section 2

12. ECOLOGICAL INFORMATION

12.1 Toxicity

No data available.

12.2 Persistence and degradability

No data available.

12.3 Bioaccumlative potential

No data available.

12.4 Mobility in soil

No data available.

12.5 Results of PBT and vPvB assessment

PBT/vPvB assessment unavailable as chemical safety assessment not required or not conducted.

12.6 Other adverse effects

No data available.

13. DISPOSAL CONSIDERATIONS

13.1 Waste treatment methods

Product

Dispose substance in accordance with prevailing country, federal, state and local regulations.

Contaminated packaging

Conduct recycling or disposal in accordance with prevailing country, federal, state and local regulations.

14. TRANSPORT INFORMATION

DOT (US)

This substance is considered to be non-hazardous for transport.

IMDG

This substance is considered to be non-hazardous for transport.

IATA

This substance is considered to be non-hazardous for transport.

15. REGULATORY INFORMATION

SARA 302 Components:

No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302.

SARA 313 Components:

This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

SARA 311/312 Hazards:

No SARA Hazards.

Massachusetts Right To Know Components:

No components are subject to the Massachusetts Right to Know Act.

Pennsylvania Right To Know Components:

No components are subject to the Pennsylvania Right to Know Act.

New Jersey Right To Know Components:

No components are subject to the New Jersey Right to Know Act.

California Prop. 65 Components:

This product does not contain any chemicals known to State of California to cause cancer, birth defects, or anyother reproductive harm.

16. OTHER INFORMATION

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

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Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA

3 CPK2017-623-06342

Catalog No : CS-0285 Batch#06342 A-RP-199 WRH

Sample Name:	**CPK2017-623-06342**	*Injection Volume:*	**5.0**
Vial Number:	**RC5**	*Channel:*	**UV_VIS_1**
Sample Type:	**unknown**	*Wavelength:*	**215**
Control Program:	**HY-252_34-1,215NM**	*Bandwidth:*	**n.a.**
Quantif. Method:	**default**	*Dilution Factor:*	**1.0000**
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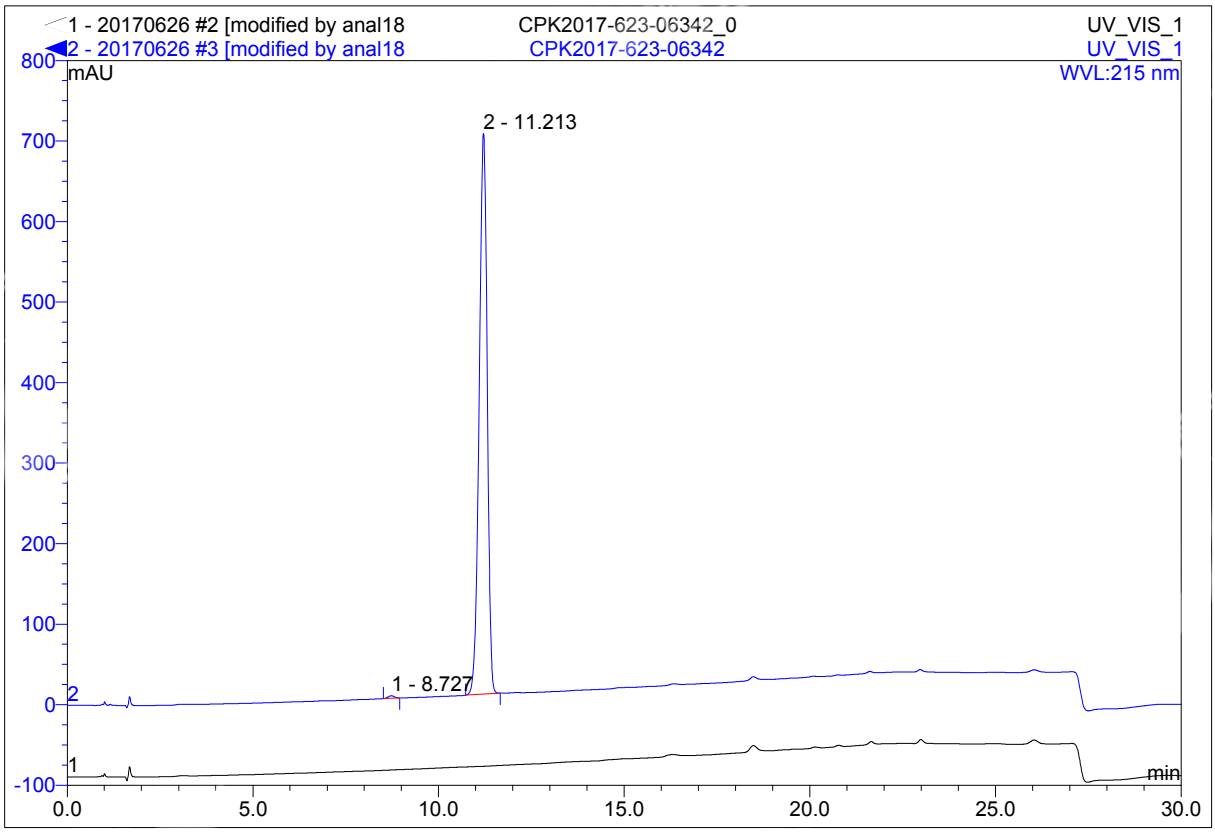
Run Time (min):	**30.00**	*Sample Amount:*	**1.0000**



No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
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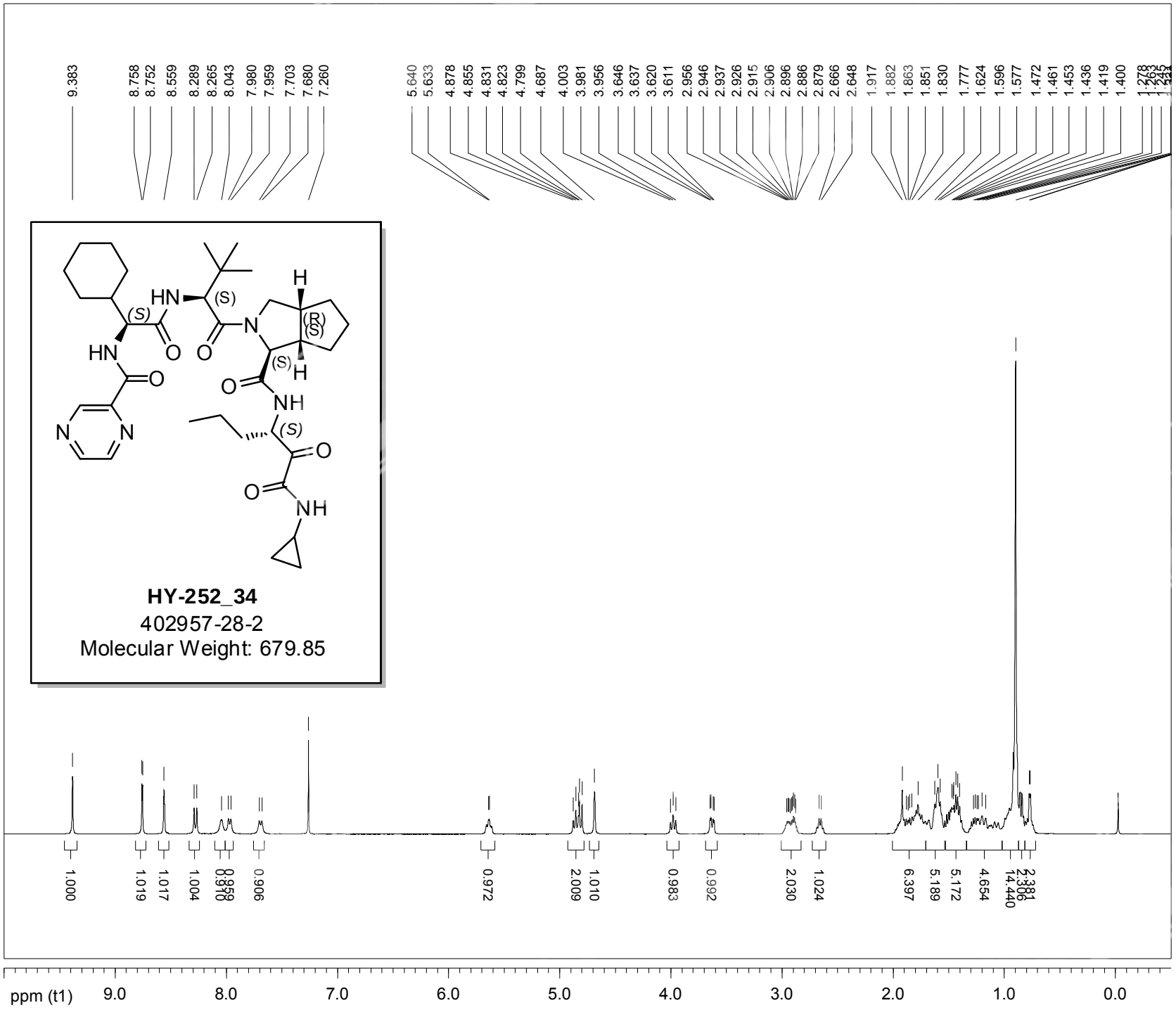
2	11.21	n.a.	696.398	174.011	99.65	n.a.	BMB*
Total:			699.470	174.624	100.00	0.000	

SampleID:CPK2017-623-06342,Catalog No : CS-0285 Batch#06342,CDCL3



Date:
26 Jun 2017
Document's Title:
Catalog No : CS-0285 Batch#06342

Spectrum Title:
CPK2017-623-06342

Frequency (MHz):
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Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown