



Avila Presents Preclinical Data on two Novel, Orally-Available Protease Inhibitors, AVL-181 and AVL-192, for Hepatitis C Infection at EASL 2010 Meeting

Inhibitors Achieve Sustained, Irreversible Silencing of HCV Protease, Potential for Best-in-Class Pan-Genotype HCV Therapeutic

VIENNA, AUSTRIA and WALTHAM, MA – April 16, 2010 – [Avila Therapeutics™, Inc.](#), a biotechnology company developing targeted [covalent drugs](#) that treat diseases through [protein silencing](#), presented results of preclinical studies on two of its [Hepatitis C Virus \(HCV\) protease inhibitors](#), AVL-181 and AVL-192. These inhibitors, due to their unique mechanism of action with superior selectivity and potency, have potential as best-in-class, pan-genotype HCV therapeutics. New data on both drugs were presented today at the 45th [Annual Meeting of the European Association for the Study of the Liver \(EASL\)](#).

AVL-181 and AVL-192 are novel, orally-available compounds that can rapidly and completely silence the HCV protease (also known as NS3) through highly selective, irreversible covalent bonding to the target protein. Clinical investigation of AVL-181 is anticipated to begin in 2010. Preclinical data have demonstrated that each drug achieves high potency and selectivity and also effectively inhibits drug-resistant mutations of HCV protease. In addition, AVL-192 has shown unusually high potency by demonstrating the ability to clear replicon cells as a monotherapy in vitro.

"We believe that our drugs, through their unique covalent mechanism, have the ability to offer a profile for a best-in-class pan-genotype HCV therapeutic. We envision that these therapies could be the backbone of a new standard of care for HCV," said Juswinder Singh, Ph.D., Chief Scientific Officer, Avila.

In a poster titled, "*AVL-192: Potency Against HCV NS3 Mutants Allows for Replicon Clearance as a Monotherapy and in Combination Studies*," (Poster #751) preclinical data demonstrate that AVL-192:

- Potently and irreversibly silences both wild-type (EC₅₀, 3.7 nM) and clinically-arising HCV protease mutants (R155K EC₅₀, 6.7 nM);
- Is highly selective and spares host proteases;
- Is curative as monotherapy in the genotype 1b replicon clearance assay at concentrations as low as 24 nM;
- Durably inhibits the HCV protease and drug resistant mutants for more than 24 hours after a single exposure; this contrasts with the need for nearly continuous exposure required by the reversible HCV protease inhibitors currently in late-stage clinical trials.

In a second poster, "*AVL-181, a Potent and Selective Irreversible HCV Protease Inhibitor, Exploits the Binding Site Microenvironment to Form a Targeted and Highly Specific Covalent Bond with CYS-159*" (Poster #764), the data show that AVL-181:

- Forms an irreversible bond with Cys159, a non-catalytic amino acid that is present in all variants of HCV protease, thus facilitating pan-genotype activity;
- Achieves uniquely selective covalent bond formation with HCV protease because of a secondary interaction with an amino acid in the Cys159 microenvironment called Lys136. The Lys136 interaction enables use in AVL-181 of targeted chemistry that uniquely bonds to Cys159 in HCV protease and does not bond to human proteases.

About [Covalent Drugs](#)

The covalent bonding mechanism of Avila Therapeutics' drugs has unique properties to effectively 'silence' disease-causing proteins. Avila drugs establish a strong and enduring 'bond' – exceeding the more temporary 'binding' of conventional drugs – to completely shut down the activity of, and silence, a disease-causing protein. Avila's covalent drugs inherently provide prolonged duration of action through this silencing of the disease target, and they have the potential for unique therapeutic benefits because they are exquisitely targeted and are effective against mutations.

About [Avila Therapeutics](#)

Avila focuses on design and development of targeted covalent drugs to achieve best-in-class outcomes that cannot be achieved through traditional chemistries. This approach is called "protein silencing". The company's product pipeline has been built using its proprietary Avilomics™ platform and is currently focused on viral infection, cancer and autoimmune disease. Avila is funded by leading venture capital firms: Abingworth, Advent Venture Partners, Atlas Venture, Novartis Option Fund, and Polaris Venture Partners. For additional information, please visit <http://www.avilatx.com>.