



Avila Presents Preclinical Data on a Novel, Orally-Available, Protease Inhibitor, AVL181, for Hepatitis C Infection at EASL 2009 Meeting

AVL-181 Has Unique Mechanism of Action for Achieving Sustained, Irreversible Silencing of Hepatitis C Virus Protease

COPENHAGEN, DENMARK and WALTHAM, MA – April 25, 2009 – Avila Therapeutics™, Inc., a biotechnology company developing novel covalent drugs that treat diseases through protein silencing, for the first time presented results of preclinical studies on its small molecule Hepatitis C Virus (HCV) protease inhibitor, AVL-181, that show AVL-181 bonds covalently and irreversibly to HCV protease (also known as “NS3”), thus silencing a key protein necessary for the virus to replicate. The data also show AVL-181 demonstrates activity *in vitro* with a longer duration of action and better activity against clinically-relevant mutations than other newly emerging therapies for HCV infection. Additionally, the data demonstrate that the amount of HCV protease silenced by AVL-181 can be measured in a dose- and time-dependent manner using Avila’s newly developed translational technologies. The translational approach can now be applied to a novel animal model presented by Avila for the testing of AVL-181 *in vivo*. These data were presented today at the 44th Annual Meeting of the European Association for the Study of the Liver (EASL).

"We believe that our covalent drugs, through their unique mechanism of action, will provide a clear advantage over other approaches to HCV therapy. By potently and irreversibly silencing HCV protease in a highly selective manner, AVL-181 also retains activity against mutant viruses that can escape inhibition from other newly emerging HCV therapies," said Juswinder Singh, Ph.D., Chief Scientific Officer, Avila. "These data support clinical evaluation of our drugs in the treatment of HCV patients, and we are aggressively advancing this class of drugs into late-stage preclinical studies with the goal of entering a candidate into clinical trials in 2010."

"Furthermore, we have identified a critical site shared by all known HCV protease variants that we think could potentially be the Achilles' heel of HCV," said Dr. Singh. "AVL-181 was shown to bond irreversibly to this critical site, and we plan to further exploit this exciting new discovery through our powerful covalent platform."

In one study, "*Protein Silencing of Hepatitis C Virus Protease with a Small Molecule Inhibitor: Discovery of AVL-181*" (Abstract #962), data demonstrate that the orally available, novel HCV protease inhibitor, AVL-181:

- Potently and irreversibly silences wild-type and drug-resistant HCV protease;
- Selectively disrupts the HCV protease with no appreciable activity on host proteases thus demonstrating potential for better safety in humans;

- Durably inhibits the HCV protease and drug resistant mutants for more than 24 hours after a single exposure; this prolonged inhibition correlates with the protease half-life and contrasts with the need for nearly continuous exposure required by the reversible HCV protease inhibitors currently in late-stage clinical trials; and,
- Functions *in vivo* utilizing a novel animal model developed by Avila that allows measurement of the extent and duration of the inhibition of HCV protease activity.

In a second study, “*Protein Silencing of HCV NS3 Protease: A New Small Molecule Approach*” (Abstract #945), Avila demonstrates that covalent drug technology can potently and irreversibly silence HCV protease, including drug-resistant variants (e.g., R155K). The HCV protease has been identified as essential for viral replication and therefore has been one of the most attractive targets for developing specific antiviral agents against HCV.

Importantly, the study also elucidates two additional novel technologies unique to the Avila platform:

- An *in vitro* assay in which protease activity can be monitored in cultured cells after withdrawal of drug, and in which Avila’s covalent drugs exhibit vastly improved duration of action versus conventional small molecules currently in clinical development for HCV therapy; and,
- The development of proprietary covalent translational technology that allows the quantitative assessment of target protease that is actually occupied by drug, and that will provide a valuable translational tool for rational clinical development.

“We are excited to share with the scientific community the innovative and leading edge technologies we have developed to support our covalent platform,” said Dr. Singh. “These technologies will guide and inform both our preclinical and clinical studies and create considerable value for Avila.”

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 have unique therapeutic benefits because they are exquisitely targeted, are effective against mutations and have long duration of action.

About Avila Therapeutics

Avila Therapeutics is the only biotechnology company developing a whole new therapeutic approach called ‘protein silencing’ based on a proprietary platform for developing covalent drugs that strongly and resiliently bond to disease-causing proteins, resulting in drugs that can be highly effective against diseases. Avila’s covalent drugs have unique therapeutic benefits because they are highly targeted, are effective against mutations and have long duration of action. Avila is developing a pipeline of novel, protein silencing drugs with a current focus on viral infection, cancer, and autoimmune diseases. Avila was founded in 2007 and is based in Waltham, Massachusetts. For additional information, please visit <http://www.avilatx.com>.

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