



Avila Presents Data on its Novel, Orally-Available Protease Inhibitor, AVL-181, Demonstrating Viral Clearance of Hepatitis C Virus in Preclinical Models

Potential for Rapid and Prolonged Therapeutic Benefit in HCV through Protein Silencing of NS3 Protease

BOSTON and WALTHAM, MA – November 2, 2009 – Avila Therapeutics™, Inc., a biotechnology company developing novel covalent drugs that treat diseases through protein silencing, presented results of preclinical studies on its highly selective, small molecule Hepatitis C Virus (HCV) protease inhibitor, AVL-181. Avila showed that AVL-181 promoted complete viral clearance *in vitro* when used at clinically-relevant concentrations in combination with other HCV therapies. Additionally, using an innovative technology for measuring the extent of covalent bond formation, Avila showed that AVL-181 bonds selectively and irreversibly to HCV protease *in vivo* in a novel rodent model, thus silencing a key protein necessary for successful viral replication and resulting in a prolonged duration of action *in vivo*. These new data will be presented tomorrow at the 60th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) international meeting in Boston, Massachusetts.

"Our clinical candidate, AVL-181, demonstrated inhibition across multiple genotypes and drug-resistant mutations of the HCV protease. In addition, the data showing complete viral clearance in conjunction with other cutting edge therapies are striking," said Katrine Bosley, Chief Executive Officer, Avila. "These data provide additional support for the clinical evaluation of AVL-181, and we are on track to advance into clinical development next year."

In one presentation, "*Potential for Rapid and Prolonged Therapeutic Benefit in HCV through Protein Silencing of NS3 Protease with AVL-181*", the data show that the orally-available, novel HCV protease inhibitor, AVL-181:

- selectively bonds the HCV NS3 protease to completely and irreversibly inactivate proteolytic activity, essentially silencing the HCV protease complex;
- forms a highly specific covalent bond across HCV genotypes and clinically-described drug-resistant mutant proteases;
- inhibits protease activity in cultured replicon cells for >48 hours after very brief exposure and removal of AVL-181;
- demonstrates prolonged pharmacodynamic activity for both wild-type and drug-resistant mutations (e.g. R155K); and;
- results in clearance of HCV RNA from replicon cells in conjunction with a non-nucleoside polymerase inhibitor, contributing to a profile that differentiates AVL-181 from clinically investigated agents.

In a second presentation, “AVL-181 Demonstrates Prolonged Inhibition of HCV NS3 Protease Activity *In Vivo* that Directly Correlates with Prolonged Molecular Target Occupancy”, the data demonstrate that the orally available, novel HCV protease inhibitor, AVL-181:

- potently and irreversibly silences HCV proteases, and that the level of protease inhibition is directly correlated with the extent of target bonding;
- durably inhibits the HCV protease for at least 10 hours *in vivo* after a single exposure as measured in a novel model in which NS3/4A is expressed in the mouse liver; and
- this duration of action coupled with the low plasma levels of AVL-181 at this late timepoint confirm that the covalent mechanism does not depend on the near-continuous drug exposure such as that required by the reversible HCV protease inhibitors currently in late-stage clinical trials.

About the Avilomics™ Platform and Covalent Drugs

The Avilomics platform is Avila’s powerful approach to design and develop covalent drugs that strongly, selectively, and resiliently bond to disease-causing proteins, thereby silencing their activity and producing superior pharmacological outcomes. Covalent drugs inherently provide prolonged duration of action through this silencing of the disease target, and they can solve the critical therapeutic challenges of drugging difficult targets and addressing resistance mutations. The three components of Avilomics are:

- Compositions: Innovative chemical structures for forming highly selective, not indiscriminate, covalent bonds
- Design: Proprietary informatics to uniquely identify sites amenable to selective covalent modification and target silencing
- Testing: Empirical methods to demonstrate covalent specificity at both target and proteomic levels

Together, these components provide a platform for efficient design and testing of covalent drugs. Avilomics opens up the broad potential of covalent drugs across target classes and disease areas, as demonstrated with the company’s emerging pipeline of novel, protein silencing covalent drugs.

About Avila Therapeutics™, Inc.

Avila focuses on design and development of covalent drugs to achieve best-in-class outcomes that cannot be achieved through traditional chemistries. This approach is called “protein silencing”. The company is developing a pipeline of novel, protein-silencing covalent drugs with a current focus 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>.

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