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Theravance Biopharma Announces Positive Results From Phase 1 Proof-of-Concept Study of TD-6450, an NS5A Inhibitor to Treat Hepatitis C

240 mg Achieved a Median Maximal Viral Load Decline of 4.9 Log10 IU/mL Following Three Daily Doses in Genotype 1a Patients

SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 11/03/14 -- Theravance Biopharma (NASDAQ: TBPH), through its U.S. operating subsidiary, Theravance Biopharma US, Inc., today announced positive results from the first three cohorts of Study 0110, a Phase 1 proof-of-concept study of TD-6450, a next-generation investigational NS5A inhibitor in development to treat patients with hepatitis C virus infection (HCV).

TD-6450 was evaluated in three cohorts of eight genotype 1a (GT-1a) patients each at doses of 60, 120 and 240 mg, administered once-daily for three days. TD-6450 demonstrated dose-dependent antiviral activity with median maximal declines of HCV RNA of 3.87, 4.63 and 4.89 $\log_{10}$ IU/mL for doses of 60, 120 and 240 mg, respectively.

In the 120 and 240 mg dose groups, three days of once-daily oral treatment resulted in levels of serum HCV RNA below the limit of detection (LOD) in 43% (3/7) and 57% (4/7) of patients treated with TD-6450, respectively. Three of the seven LOD patients went on to show no measurable virus at Day 14, and two of these patients still had no measurable virus at Day 28. At a two-month time point in a long-term follow-up study, the viral load in these two patients was measurable, but both remained more than three logs below their baseline.

None of the patients in the three dose groups had virologic breakthrough during their three-day treatment course, and 100% of the treated GT-1a patients in the study achieved at least a three $\log_{10}$ IU/mL reduction of HCV RNA. At the 120 and 240 mg doses, 71% (5/7) and 86% (6/7) of treated patients achieved at least a four $\log_{10}$ IU/mL reduction in HCV RNA, respectively.

All doses of TD-6450 were generally well tolerated after three doses and for the 28-day observation period. There were no serious adverse events and no patient discontinuations. There was no pattern of clinical adverse events or laboratory abnormalities related to treatment.

"We see diverse responses to direct antivirals in genotype 1 populations. Despite recent advances in HCV therapy, significant treatment challenges remain, including the required length of drug therapy. The robust activity of TD-6450 in genotype 1a patients suggests that this potentially best-in-class NS5A inhibitor could be a component of short and highly active combination therapy regimens," said Eric Lawitz, MD, Vice President of Scientific and Research Development at the Texas Liver Institute and Clinical Professor of Medicine, The University of Texas Health Science Center San Antonio, and one of the principal investigators on the Phase 1 study.

"TD-6450, created using the principles of multivalent design, has a heterodimeric structure distinct from other NS5A inhibitors. We believe this unique structure allows it to bind asymmetrically across the NS5A protein interface, providing high *in vitro* potency against clinically encountered resistance-associated variants. We believe the potency of TD-6450 against both wild type virus and these resistance-associated variants enables the robust antiviral activity that we reported today," said Mathai Mammen, MD, Senior Vice President, Research and Development, Theravance Biopharma. "We look forward to analyzing the full set of results from this Phase 1 study and evaluating the next steps in the development strategy for TD-6450."

About the Phase 1 Proof-of-Concept Study (Study 0110)

This Phase 1 study is a double-blind, randomized, placebo-controlled, multiple-dose study to evaluate the safety, tolerability, pharmacokinetics and antiviral activity of orally administered TD-6450 in non-cirrhotic, treatment-naive patients with GT-1, 2, or 3 chronic HCV infection. The study includes seven cohorts. The first three cohorts enrolled eight GT-1a patients each (7 active; 1 placebo) and tested once-daily oral doses of 60, 120 or 240 mg, respectively. Patients were dosed for three days and followed for up to 28 days for viral load quantification. The limit of detection for the viral load quantification assay is 15 IU/mL.

Safety evaluations include monitoring for adverse events, routine laboratory assessments, vital signs and 12-lead ECG tracings.

In cohorts 4 through 6, patients with GT-1b, GT-2 and GT-3 are dosed once-daily at 240 mg. An additional cohort (cohort 7) of GT-1a patients is dosed twice daily with 240 mg. Data generation and analysis of results for cohorts 4 through 7 is ongoing. An interim analysis of those cohorts showed antiviral activity for GT-1b similar to that for GT-1a, but minimal antiviral activity for GT-2 and GT-3.

The Company anticipates presenting further data on all cohorts at a future scientific conference.

About TD-6450

TD-6450 is an internally discovered multivalent NS5A inhibitor designed to have improved antiviral activity against GT-1 resistance-associated variants (RAV) resistant to first generation NS5A inhibitors. TD-6450's heterodimeric structure permits an asymmetric binding mode to NS5A relative to structurally symmetric inhibitors. TD-6450 has demonstrated additive activity with other classes of anti-HCV agents in replicon assays, and no cross-resistance with RAVs that confer resistance to other anti-HCV agents. The Company believes that the antiviral activity of TD-6450, in combination with other antivirals, may help improve cure rates and/or reduce treatment times for appropriate patients.

TD-6450 was previously evaluated in a single-ascending dose and a 14-day multiple-ascending dose study in healthy subjects (study 0094). This randomized, double-blind, placebo-controlled study evaluated the safety, tolerability and pharmacokinetics of TD-6450. Single doses (up to 500 mg) and multiple doses of TD-6450 (up to 240 mg daily for 14 days) were evaluated in healthy subjects. Following single and multiple doses, TD-6450 was generally well-tolerated and no subjects discontinued due to adverse events. Headache was the most commonly reported adverse event following multiple doses (n=4). TD-6450 pharmacokinetics were linear up to 240 mg following single and multiple doses and its long half-life supports once-daily dosing.

About Hepatitis C and the NS5A Inhibitor Class

Hepatitis C is an infectious disease of the liver. Worldwide, health experts estimate that 130 - 150 million people have chronic hepatitis C, with as many as four million of those cases in the United States. Hepatitis C, like all forms of hepatitis, can damage the liver. Of people infected, 55 to 85 percent will develop chronic infection, and 75 percent of those with chronic infection will develop chronic liver disease.

The hepatitis C non-structural 5A (NS5A) protein of HCV has emerged as an attractive drug target and inhibitors of NS5A have a central role in all-oral HCV therapy. The multi-functional NS5A protein is required for ribonucleic acid (RNA) replication and virion assembly, and a number of investigational and approved NS5A inhibitors have shown antiviral efficacy in HCV-infected patients.

Conference Call Today at 5:00 pm ET

Theravance Biopharma will hold a conference call today at 5:00 pm ET to discuss the results of the Phase 1 study of TD-6450. To participate in the live call by telephone, please dial (855) 296-9648 from the US, or (920) 663-6266 for international callers. To listen to the conference call live via the internet, please visit Theravance Biopharma's web site at www.theravance.com, under the Investor Relations section, Presentations and Events. To listen to the live call and to download the slide presentation, please go to Theravance Biopharma's web site 15 minutes prior to its start to register, download, and install any necessary audio software.

A replay of the conference call will be available on Theravance Biopharma's web site for 30 days through December 3, 2014. An audio replay will also be available through 11:59 p.m. ET on November 10, 2014 by dialing (855) 859-2056 from the US, or (404) 537-3406 for international callers, and entering confirmation code 28908270.

About Theravance Biopharma

Theravance Biopharma is a biopharmaceutical company focused on the discovery, development and commercialization of small molecule medicines across a number of therapeutic areas, including respiratory disease, bacterial infections, central nervous system (CNS)/pain, and gastrointestinal (GI) motility dysfunction. Theravance Biopharma has one approved product, VIBATIV® (telavancin), which was discovered and developed internally, a pipeline of internally discovered product candidates and strategic collaborations with pharmaceutical companies. In addition, the Company has an economic interest in future payments that may be made by GlaxoSmithKline plc (GSK) pursuant to its agreements with Theravance, Inc. relating to certain drug programs, including the combination of fluticasone furoate (FF), umeclidinium (UMEC), and vilanterol (VI) (FF/UMEC/VI), the combination of the bifunctional muscarinic antagonist-beta$_2$ agonist (MABA) GSK961081 ('081) and FF ('081/FF), and MABA monotherapy. By leveraging its proprietary insight of multivalency to drug discovery, the Company is pursuing a best-in-class strategy designed to discover superior medicines in areas of significant unmet medical need.

Theravance Biopharma is a publicly-held corporation, with U.S. headquarters located in South San Francisco, California, and

trades on the NASDAQ Global Select Market under the symbol TBPH. For additional information, please visit www.theravance.com.

This press release contains and the conference call will contain certain "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives and future events. Theravance Biopharma intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to: the strategies, plans and objectives of Theravance Biopharma, the status and timing of clinical studies, data analysis and communication of results, the potential benefits and mechanisms of action of product candidates, the enabling capabilities of Theravance Biopharma's approach to drug discovery and Theravance Biopharma's proprietary insights, expectations for product candidates through development and commercialization (including their potential as components of combination therapies), and the timing of seeking regulatory approval of product candidates. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of the press release and the conference call and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance Biopharma to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, risks related to: the disruption of operations during the transition period following the spin-off of Theravance Biopharma from Theravance, Inc., including the diversion of management's and employees' attention from the business, adverse impacts upon the progress of discovery and development efforts, disruption of relationships with collaborators and increased employee turnover, delays or difficulties in commencing or completing clinical studies, the potential that results from clinical or non-clinical studies indicate product candidates are unsafe or ineffective (including when our product candidates are studied in combination with other compounds), dependence on third parties to conduct clinical studies, delays or failure to achieve and maintain regulatory approvals for product candidates, risks of collaborating with third parties to discover, develop and commercialize products and risks associated with establishing distribution capabilities for telavancin with appropriate technical expertise and supporting infrastructure. Other risks affecting Theravance Biopharma are described under the heading "Risk Factors" contained in Theravance Biopharma's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 14, 2014. In addition to the risks described above and in Theravance Biopharma's other filings with the SEC, other unknown or unpredictable factors also could affect Theravance Biopharma's results. No forward-looking statements can be guaranteed and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance Biopharma assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.

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