

Theravance Biopharma Announces Positive Top-Line Results from Phase 2b Dose-Ranging Study of its Investigational LAMA, TD-4208, for the Treatment of COPD

Primary and Secondary Efficacy Endpoints Met for Doses 88 mcg and Above; TD-4208 Demonstrates Clear Dose-Response Relationship and FEV₁ Profile Consistent with Once-Daily Dosing

SOUTH SAN FRANCISCO, CA -- (Marketwired) -- 09/08/14 -- Theravance Biopharma (NASDAQ: TBPH), through its US operating subsidiary, Theravance Biopharma US, Inc., today announced positive top-line results from its Phase 2b dose-ranging study of TD-4208, an investigational long-acting muscarinic antagonist (LAMA) in development for the treatment of chronic obstructive pulmonary disease (COPD). The study evaluated four doses of TD-4208 (44, 88, 175 and 350 mcg) and placebo, administered once daily for 28 days in a double-blind, parallel group study in a total of 355 patients with moderate-to-severe COPD.

TD-4208 met the primary efficacy endpoint (change from baseline in trough FEV₁ [forced expiratory volume in one second] following the last dose on Day 28) at once-daily doses of 88, 175 and 350 mcg, with statistically significant changes versus placebo ($p < 0.001$) in trough FEV₁ of 187 mL, 167 mL and 171 mL, respectively. The lowest dose of 44 mcg produced a sub-therapeutic response of 52 mL that was not statistically different from placebo.

"For those COPD patients who depend on nebulized treatment to manage their COPD, currently available therapies require dosing more than once per day," said Brett Haumann, MD, Vice President, Clinical Development and Operations. "These Phase 2b results show that TD-4208 has the potential to provide these patients with a once-daily, efficacious and well tolerated therapeutic option."

Analyses of secondary endpoints were positive and consistent with the primary endpoint for doses of 88 mcg and above (all nominal p -values < 0.01 versus placebo). TD-4208 doses of 88, 175 and 350 mcg resulted in a placebo-corrected change from baseline on Day 28 in the 0 to 24-hour weighted mean FEV₁ of 165, 162 and 174 mL, respectively. TD-4208 doses of 88 mcg and above showed a rapid onset of action as measured by a median time of 30 minutes to a 100 mL increase from baseline on Day 1. Doses of 88 mcg and above reduced the use of rescue medication by more than 1 puff per day, compared to placebo.

TD-4208 was generally well tolerated. Headache, shortness of breath and cough were the most common adverse events in the study, reported in 11 (3.1%), 10 (2.8%) and 7 (2.0%) subjects, respectively. Notably, there were minimal reports of side effects associated with anti-cholinergic treatment: there were only 2 reports of dry mouth, and no reports of blurred vision, constipation or urinary retention. Four subjects experienced serious adverse events, three of which were considered to be unrelated to study treatment by the blinded investigators, and the fourth was considered unlikely to be related to study treatment by the blinded expert reviewer. The overall withdrawal rate in the study was under 10%. A greater number of patients prematurely discontinued the study due to treatment-emergent adverse events in the two highest dose groups. Review of laboratory panels revealed no abnormal trends.

Commented Rick E Winningham, Chief Executive Officer: "We believe that TD-4208 has the potential to be a best-in-class single-agent product for COPD patients who require nebulized therapy. In addition, the therapeutic profile, together with the physical characteristics of TD-4208, suggest that this LAMA could serve as a foundation for several combination products and for delivery in metered dose inhaler and dry powder inhaler products. TD-4208 represents an important opportunity for our Company."

Theravance Biopharma anticipates completing a once- versus twice-daily study of TD-4208 in the fourth quarter of 2014, with the goal of further confirming the suitability of once-daily dosing. Taken together, the data from this Phase 2b study and the once- versus twice-daily study should enable the Company to seek an end-of-Phase-2 meeting with the FDA to discuss the pathway to a registrational Phase 3 program.

About the Phase 2b Study

The objectives of this randomized, double-blind, multicenter, placebo-controlled Phase 2b study were to characterize the FEV₁ dose-response relationship, pharmacokinetics, safety and tolerability of multiple doses of TD-4208 in patients with moderate-to-severe COPD.

The study was conducted at 41 clinical sites in the US. A total of 355 patients were randomized to receive one of four doses of TD-4208 (44, 88, 175 or 350 mcg) or placebo once daily via a nebulizer in a 28-day, double-blind, parallel-group study design. Subjects had an average age of 62 years, a minimum of a 10 pack-year smoking history and an average FEV₁ % predicted of 44%. Thirty-seven percent of subjects were on inhaled corticosteroids, and 35% of subjects had irreversible airways disease at screening.

The primary efficacy endpoint of the study was change from baseline in trough FEV₁ after the last dose of treatment on Day 28. Secondary endpoints included trough FEV₁ on Day 15, 16 and 28, weighted mean (area under the curve) assessments of FEV₁ from 0 to 6 hours on Day 1 and 0 to 24 hours on Day 28, rescue medication use and peak expiratory flow.

Safety evaluations included adverse events, routine laboratory assessments, vital signs, 12-lead ECG tracings and 24-hour Holter ECG profiles. A subset of subjects in each treatment arm provided blood samples for pharmacokinetic evaluation.

About TD-4208 and the LAMA Program

TD-4208 is an investigational inhaled, long-acting muscarinic antagonist (LAMA) discovered by the team at Theravance Biopharma through the application of multivalent design to muscarinic receptors in a drug discovery program dedicated to finding new medicines for respiratory diseases, such as COPD and asthma. TD-4208 was designed to have high specificity for muscarinic receptors, a long receptor half-life, sustained activity in the lung after inhalation and minimal effects outside of the lung. In a previously reported Phase 2a study, doses of 350 and 700 mcg of nebulized TD-4208 demonstrated sustained bronchodilation over 24 hours and an onset of action similar to that of ipratropium, which was included as an active comparator. In a previously reported Phase 2b study, doses of 22, 44, 88, 175 and 350 mcg of nebulized TD-4208 demonstrated dose-related efficacy versus placebo, with doses of 22 and 44 mcg showing sub-effective efficacy following 7 days of dosing.

About COPD

More than 12.5 million US adults are estimated to have COPD, and it is currently the third leading cause of death in the US, with more than 130,000 deaths annually. Smoking is the primary risk factor, and more than 80% of COPD deaths are caused by smoking. People who smoke are 12-13 times more likely to die from COPD than people who have never smoked. Other risk factors include air pollution, passive smoking, occupational exposure and genetic factors. More than 700,000 patients are admitted to hospitals annually in the US with worsening of their COPD. The costs of managing COPD in the US were estimated to be \$50 billion in 2010, including \$29.5 billion in direct health care expenditures, \$8.0 billion in indirect morbidity costs and \$12.4 billion in indirect mortality costs. An American Lung Association survey revealed that half of all COPD patients (51%) say their condition limits their ability to work. It also limits them in normal physical exertion (70%), household chores (56%), social activities (53%), sleeping (50%) and family activities (46%).

Source: American Lung Association

<http://www.lung.org/lung-disease/copd/resources/facts-figures/COPD-Fact-Sheet.html>

Conference Call Today at 5:00 pm EDT

Theravance Biopharma will hold a conference call today at 5:00 pm EDT to discuss the results of the Phase 2b study of TD-4208. To participate in the live call by telephone, please dial (877) 837-3908 from the US, or (973) 890-8166 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's 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 October 8, 2014. An audio replay will also be available through 11:59 p.m. Eastern Daylight Time on September 15, 2014 by dialing (855) 859-2056 from the US, or (404) 537-3406 for international callers, and entering confirmation code 1820744.

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-beta₂ 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.

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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, 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, 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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Source: Theravance Biopharma

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