



## **Theravance Announces Positive Results from a Phase 2a Study of its LAMA Candidate, TD-4208, for the Treatment of COPD**

**SOUTH SAN FRANCISCO, CA/November 14, 2011** – Theravance, Inc. (NASDAQ: THRX) announced today positive topline results from a Phase 2a single-dose study of TD-4208, an investigational inhaled long-acting muscarinic antagonist (LAMA), discovered using Theravance’s multivalent approach to drug design. This compound is under development by Theravance for the treatment of chronic obstructive pulmonary disease (COPD). In this study, TD-4208 met the primary endpoint by demonstrating a statistically significant mean change from baseline in peak forced expiratory volume in one second (FEV<sub>1</sub>) compared to placebo and was generally well tolerated.

“We are encouraged by these positive Phase 2a results, which support further development of TD-4208 in COPD,” said Mathai Mammen, Sr. Vice President, Research and Early Clinical Development of Theravance. “We designed TD-4208 to be a multivalent antagonist with high specificity for muscarinic receptors, sustained activity in the lung after inhalation, and minimal effects outside of the lung. We are excited that our core technology continues to yield promising clinical candidates for patients with significant medical needs.”

In the recently completed Phase 2a study, both doses of TD-4208 (350 mcg and 700 mcg) and the active control ipratropium bromide (500 mcg, the marketed dose), each administered via nebulizer, demonstrated a statistically significant improvement in peak FEV<sub>1</sub> versus placebo of 174 mL (95% Confidence Interval (CI): 112, 235), 169 mL (95% CI: 108, 231) and 176 mL (95% CI: 114, 237), respectively, with  $p < 0.001$ . All three treatments demonstrated a rapid and similar onset of action. In a secondary analysis, both doses of TD-4208 demonstrated a long duration of action with statistically significant effect at 24 hours. The mean changes from baseline in FEV<sub>1</sub> compared to placebo at 24 hours were 103 mL and 137 mL for 350 mcg and 700 mcg of TD-4208, respectively. As expected, ipratropium bromide did not produce significant effects versus placebo at 12 hours and 24 hours.

Both doses of TD-4208 were generally well tolerated in the study with an incidence of adverse events similar to those for ipratropium bromide and placebo and with no clinically significant increase in heart rate or evidence of dry mouth. Adverse events were generally mild and occurred in all treatment and placebo groups with the most common adverse events being headache and dyspnea. There were no serious adverse events reported in the study. The full results of the study will be presented at an upcoming medical conference.

### **About the Phase 2a Study**

The objectives of this Phase 2a randomized, double-blind, four-period crossover study were to evaluate the bronchodilatory effect, pharmacokinetics, safety and tolerability of single inhaled doses of TD-4208 in patients with COPD. A total of 32 patients outside of the United States, 40-75 years of age, with moderate to severe COPD (FEV<sub>1</sub> 35 – 80% predicted, FEV<sub>1</sub>/FVC <0.7) were randomized to receive TD-4208 (350 mcg and 700 mcg), ipratropium bromide, and placebo, each administered as single doses via a nebulizer. All patients received each of the four treatments. The primary endpoint of the study was mean change from baseline in peak FEV<sub>1</sub> compared to placebo. Secondary endpoints



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included safety and tolerability, as well as additional pharmacodynamic endpoints from spirometry including area under the FEV<sub>1</sub> versus time curve (0–12 hours, 0–24 hours), FEV<sub>1</sub> value at 12 and 24 hours post dose (trough) and peak FEV<sub>1</sub> time-matched difference from placebo.

### **About TD-4208 and the LAMA Program**

TD-4208 is an inhaled, long-acting muscarinic antagonist (LAMA) discovered by Theravance through the application of multivalent design in a drug discovery program dedicated to finding new medicines for respiratory diseases such as COPD and asthma. The goal of Theravance's LAMA program is to develop a once-daily inhaled medicine that offers improved efficacy and tolerability relative to current therapies with the option to combine this medicine with other therapeutic agents for optimized combination products. To accomplish this we are developing a chemically-stable inhaled LAMA that produces prolonged blockade of the relevant muscarinic receptor sub-types in the lung while also being highly selective for lung tissue over salivary gland tissue.

### **About Theravance**

Theravance is a biopharmaceutical company with a pipeline of internally discovered product candidates and strategic collaborations with pharmaceutical companies. Theravance is focused on the discovery, development and commercialization of small molecule medicines across a number of therapeutic areas including respiratory disease, bacterial infections, and central nervous system (CNS)/pain. The Company's key programs include: RELOVAIR<sup>™</sup>, LAMA/LABA ('719/vilanterol (VI)) and MABA (Bifunctional Muscarinic Antagonist-Beta<sub>2</sub> Agonist), each partnered with GlaxoSmithKline plc, and its oral Peripheral Mu Opioid Receptor Antagonist (PμMA) program. By leveraging its proprietary insight of multivalency to drug discovery, Theravance is pursuing a best-in-class strategy designed to discover superior medicines in areas of significant unmet medical need. For more information, please visit the company's web site at [www.theravance.com](http://www.theravance.com).

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This press release contains 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 intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Exchange Act and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to the timing of clinical studies, statements regarding the potential benefits and mechanisms of action of drug candidates, statements concerning the timing of seeking regulatory approval of our product candidates, statements concerning enabling capabilities of Theravance's approach to drug discovery and its proprietary insights, and statements regarding expectations for product candidates through development and commercialization. These statements are based on the current estimates and assumptions of the management of Theravance as of the date of this press release and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance to be materially different from those reflected in its 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



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delays or difficulties in commencing or completing clinical studies, the potential that results of clinical or preclinical studies indicate product candidates are unsafe or ineffective, our dependence on third parties in the conduct of our clinical studies, delays or failure to achieve regulatory approvals for product candidates, risks of relying on third-party manufacturers for the supply of our product and product candidates and risks of collaborating with third parties to develop and commercialize products. These and other risks are described in greater detail under the heading "Risk Factors" contained in Theravance's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 2, 2011 and the risks discussed in our other period filings with SEC. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance assumes no obligation to update its forward-looking statements.

**Contact Information:**

Michael W. Aguiar  
Senior Vice President and Chief Financial Officer  
650-808-4100  
[investor.relations@theravance.com](mailto:investor.relations@theravance.com)