Theravance Biopharma Announces Dosing of First Patient in Phase 2 Allergen Challenge Study of TD-8236, an Investigational, Lung-Selective, Inhaled Pan-Janus Kinase (JAK) Inhibitor for Inflammatory Lung Diseases

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Novel Organ-Selective Pan-JAK Inhibitor Specifically Designed to Target Airway Inflammation in the Lung With Minimal Systemic Exposure

Allergen Challenge Study Expected to Provide Key Insights to Support Ongoing Clinical Development of TD-8236

DUBLIN, Dec. 3, 2019 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company") today announced dosing of the first patient in a Phase 2 allergen challenge study of TD-8236, an investigational, lung-selective inhaled pan-Janus kinase (JAK) inhibitor for inflammatory lung diseases. TD-8236 is specifically designed to target airway inflammation in the lung with minimal systemic exposure and be delivered to the lung via dry powder inhalation.

The Phase 2 trial is a randomized, double-blind, placebo-controlled, crossover allergen challenge study designed to evaluate two doses of TD-8236 compared to placebo in 21 patients with mild asthma following an inhaled allergen challenge. The primary objective of the study will be characterization of the late asthmatic response (LAR) after inhaled allergen challenge following 14 days of TD-8236 (inhaled once daily) or matched placebo. Secondary objectives of the study will include safety, tolerability, and PK assessments.

"The initiation of this allergen challenge study represents a key milestone in our development of TD-8236, a novel lung-selective pan-JAK inhibitor designed for the treatment of patients with moderate to severe asthma who are not controlled with existing inhaled corticosteroid therapy," said Brett Haumann, MD, chief medical officer of Theravance Biopharma. "Allergen challenge studies provide a well-established proof-of-concept, correlating with a broader set of clinical responses in later studies in patients with asthma. As such, we expect this trial will build upon the findings from our Phase 1 study and provide key additional insights that will further inform our future clinical trials for TD-8236."

Theravance Biopharma recently announced positive results from a Phase 1 trial of TD-8236 in healthy subjects and mild asthmatics. Study data demonstrated TD-8236 to be generally well tolerated with minimal systemic exposure, which is consistent with data from preclinical studies and the organ-selective design of the compound. Additionally, the study demonstrated reductions in fractional exhaled nitric oxide (FeNO) in patients with mild asthma and elevated FeNO levels at baseline. FeNO is an established disease activity biomarker in asthma, and reductions in FeNO are associated with a decrease in airway inflammation.

An extension (Part C) of the Phase 1 trial designed to assess a range of additional biomarkers in patients with more severe asthma continues in parallel with this new allergen challenge study. This biomarker extension is designed to further evaluate the potential impact of TD-8236 in the disease population that may be most likely to benefit from this therapy. Results from the Part C extension of the Phase 1 trial are expected in the first half of 2020.

About TD-8236 and Organ-Selective Pan-Janus (JAK) Kinase Inhibition

Theravance Biopharma is focused on utilizing organ-selective JAK inhibitors for potential treatment of a range of inflammatory lung diseases, including asthma. JAK inhibitors function by inhibiting the activity of one or more of the Janus kinase family of enzymes (JAK1, JAK2, JAK3, TYK2) that play a key role in cytokine signaling. Inhibiting these JAK enzymes interferes with the JAK/STAT signaling pathway and, in turn, modulates the activity of a wide range of pro-inflammatory cytokines. While orally-administered JAK inhibitors are currently approved for the treatment of a range of inflammatory diseases, no inhaled JAK inhibitor is approved for the treatment of airway disease, including asthma.

TD-8236 is an internally-discovered, lung-selective inhaled pan-JAK inhibitor that has demonstrated a high affinity for each of the JAK family of enzymes. The pan-JAK activity of TD-8236 suggests that it may impact a broad range of cytokines that have been associated both Th2-high and Th2-low asthma. Many moderate to severe asthma patients comprising these phenotypes remain symptomatic with currently available therapies. Importantly, TD-8236 is designed to distribute adequately and predominantly within the lungs following dry powder inhalation, with the potential to treat inflammation within that organ while minimizing systemic exposure.

About Theravance Biopharma

Theravance Biopharma, Inc. ("Theravance Biopharma") is a diversified biopharmaceutical company primarily focused on the discovery, development and commercialization of organ-selective medicines. Our purpose is to create transformational medicines to improve the lives of patients suffering from serious illnesses. Our research is focused in the areas of inflammation and immunology.

In pursuit of our purpose, we apply insights and innovation at each stage of our business and utilize our internal capabilities and those of partners around the world. We apply organ-selective expertise to biologically compelling targets to discover and develop medicines designed to treat underserved localized diseases and to limit systemic exposure, in order to maximize patient benefit and minimize risk. These efforts leverage years of experience in developing lung-selective medicines to treat respiratory disease, including FDA-approved YUPELRI® (revefenacin) inhalation solution indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Our pipeline of internally discovered programs is targeted to address significant patient needs.

We have an economic interest in potential future payments from Glaxo Group Limited or one of its affiliates (GSK) pursuant to its agreements with Innoviva, Inc. relating to certain programs, including TRELEGY ELLIPTA.

For more 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, expectations 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 Company's strategies, plans and objectives, the Company's regulatory strategies and timing of clinical studies (including the data therefrom), the potential characteristics, benefits and mechanisms of action of the Company's product and product candidates, the potential that the Company's research programs will progress product candidates into the clinic, the Company's expectations for product candidates through development, potential regulatory approval and commercialization (including their differentiation from other products or potential products), product sales or profit share revenue and the Company's expectations for its 2019 operating loss, excluding share-based compensation. 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: potential future disagreements with Innoviva, Inc. and TRC LLC, the uncertainty of arbitration and litigation and the possibility that an arbitration award or litigation result could be adverse to the Company, delays or difficulties in commencing, enrolling or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's compounds or product candidates are unsafe or ineffective, risks that product candidates do not obtain approval from regulatory authorities, the feasibility of undertaking future clinical trials for our product candidates based on policies and feedback from regulatory authorities, dependence on third parties to conduct clinical studies, delays or failure to achieve and maintain regulatory approvals for product candidates, risks of collaborating with or relying on third parties to discover, develop, manufacture and commercialize products, and risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure. Other risks affecting Theravance Biopharma are described under the heading "Risk Factors" contained in Theravance Biopharma's Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 8, 2019 and Theravance Biopharma's other filings with the SEC. In addition to the risks described above and in Theravance Biopharma's 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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