Theravance Biopharma Announces First Subject Dosed in Phase 1 Clinical Trial of TD-8236, a Novel Inhaled pan-JAK Inhibitor

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First-in-Human Study for Novel, Inhaled, Lung-Selective pan-Janus Kinase (JAK) Inhibitor with Potentially Broad Activity Across Range of Serious Respiratory Diseases

DUBLIN, Nov. 27, 2018 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company") today announced dosing of the first subject in a Phase 1 clinical trial of TD-8236, a novel, inhaled, lung-selective pan-Janus kinase (JAK) inhibitor which has demonstrated potency in preclinical assessments. The Company is developing TD-8236 as an investigational compound with the potential to treat a range of serious respiratory diseases.

TD-8236 is an internally-discovered JAK inhibitor that has demonstrated a high affinity and selectivity for each of the JAK family enzymes (JAK1, JAK2, JAK3 and TYK2). Through the inhibition of these kinases, TD-8236 interferes with the JAK/STAT signaling pathway and, in turn, modulates the activity of a wide range of pro-inflammatory cytokines. Importantly, TD-8236 is specifically designed to be an inhaled treatment for delivery to the lungs via a dry-powder inhaler with minimal systemic exposure. With multiple JAK-dependent pathways clinically validated in asthma and chronic obstructive pulmonary disease (COPD), Theravance Biopharma believes the compound offers potentially broad activity across a range of respiratory indications and patient phenotypes. TD-8236 is Theravance Biopharma's second internally-discovered JAK inhibitor to advance into clinical studies.

The Phase 1 trial is a randomized, double-blind, placebo-controlled study consisting of two parts. Part A will evaluate single ascending doses (SAD) of TD-8236 in healthy subjects, with the primary objective of assessing safety, tolerability and pharmacokinetics (PK) in this population. Part B will evaluate multiple ascending doses (MAD) of TD-8236 in patients with mild, stable asthma, with the primary objective of assessing safety, tolerability and PK in this population. Key secondary objectives of the trial will include exploratory pharmacodynamic (PD) endpoints with the goal of establishing preliminary dose response relationships in patients with mild stable asthma.

"The advancement of our lung-selective JAK inhibitor program into first-in-human clinical studies is another key milestone for our research efforts in JAK inhibition and localized medicines for localized diseases. As with TD-1473, our gut-selective pan-JAK inhibitor for inflammatory intestinal diseases, we believe that TD-8236 can address key unmet needs by delivering the proven therapeutic activity of JAK inhibition to targeted tissues without immunosuppressive liabilities associated with systemic exposure," said Brett Haumann, MD, chief medical officer of Theravance Biopharma. "In addition to its lung-selective activity, TD-8236 offers potential utility in asthma patients regardless of Th2 phenotype. As such, we expect this compound can potentially address a very broad range of the asthma patient population, many of whom are in significant need of a treatment capable of controlling their symptoms and preventing disease exacerbations."

Preclinical studies have demonstrated that treatment with TD-8236 results in long residence time and duration of action in the lung and low plasma levels, suggesting a profile suitable for once-daily treatment with minimal systemic exposure. Furthermore, TD-8236 demonstrated broad inhibition of key JAK/STAT cytokines in disease-relevant models, providing support for the biological rationale for the compound's development in asthma patients independent of their Th2, eosinophil or periostin status.

About Lung-Selective Pan-Janus (JAK) Kinase Inhibition

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. JAK inhibitors are currently approved for the treatment of diseases such as rheumatoid arthritis and myelofibrosis, though none are currently approved for the treatment of respiratory diseases such as asthma. Approved JAK inhibitors are known to have side effects associated with their systemic exposure.

TD-8236 is an internally-discovered JAK inhibitor that has demonstrated a high affinity for each of the JAK family of enzymes. Importantly, TD-8236 is a lung-selective treatment specifically designed to distribute adequately and predominantly to the lung, treating inflammation in those tissues while minimizing its systemic exposure. Theravance Biopharma is focused on utilizing targeted JAK inhibitors for potential treatment of a range of serious respiratory diseases including asthma and chronic obstructive pulmonary disease (COPD), which affect roughly 25 million and 16 million patients in the United States, respectively.[1, 2]

About Theravance Biopharma

Theravance Biopharma, Inc. ("Theravance Biopharma") is a diversified biopharmaceutical company with the core purpose of creating medicines that help improve the lives of patients suffering from serious illness.

In our relentless pursuit of this objective, we strive to apply insight and innovation at each stage of our business, including research, development and commercialization, and utilize both internal capabilities and those of partners around the world. Our research efforts are focused in the areas of inflammation and immunology. Our research goal is to design localized medicines that target diseased tissues, without systemic exposure, in order to maximize patient benefit and minimize risk. These efforts leverage years of experience in developing localized medicines for the lungs to treat respiratory disease. The first potential medicine to emerge from our research focus on immunology and localized treatments is an oral, gut-selective pan-Janus kinase (JAK) inhibitor, currently in development to treat a range of inflammatory intestinal diseases. Our pipeline of internally discovered product candidates will continue to evolve with the goal of creating transformational medicines to address the significant needs of patients.

In addition, we have an economic interest in future payments that may be made by Glaxo Group or one of its affiliates (GSK) pursuant to its

agreements with Innoviva, Inc. relating to certain programs, including Trelegy Ellipta.

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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, 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 benefits and mechanisms of action of the Company's product and product candidates, the Company's expectations for product candidates through development and potential regulatory approval and commercialization (including their potential as components of combination therapies). These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of the press release 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: delays or difficulties in commencing, enrolling or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's product candidates are unsafe or ineffective (including when our product candidates are studied in combination with other compounds), 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 and risks of collaborating with or relying on third parties to discover, develop, manufacture and commercialize products. Other risks affecting Theravance Biopharma are described under the heading "Risk Factors" contained in Theravance Biopharma'sForm 10-Q filed with the Securities and Exchange Commission (SEC) on November 8, 2018and 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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