Theravance Biopharma Announces First Subject Dosed in Phase 1 Study of TD-0903, in Development for the Treatment of Hospitalized Patients with Acute Lung Injury Caused by COVID-19

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DUBLIN and SOUTH SAN FRANCISCO, Calif., April 23, 2020 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company"), a diversified biopharmaceutical company primarily focused on the discovery, development and commercialization of organ-selective medicines, today announced that the first healthy volunteer has been dosed in a Phase 1 study of TD-0903. TD-0903 is a lung-selective, nebulized Janus kinase inhibitor (JAKi) in development for the potential treatment of hospitalized patients with Acute Lung Injury (ALI) caused by COVID-19. The Company believes TD-0903 has the potential to inhibit the cytokine storm associated with ALI and prevent progression to Acute Respiratory Distress Syndrome (ARDS).

Theravance Biopharma received approval of TD-0903's initial Clinical Trial Application (CTA) in the United Kingdom (UK) for the Phase 1 study. The purpose of this study is to assess the safety, tolerability and pharmacokinetics of single- and multiple-ascending doses (SAD/MAD) of TD-0903 in healthy volunteers and will enroll up to 54 volunteers. More information can be found on clinicaltrials.gov, identifier number: NCT04350736. Upon regulatory review and approval, the program will then initially move to a nested Phase 2 study in hospitalized patients with COVID-19 in the same clinical setting in the UK.

"Theravance Biopharma's efforts to address COVID-19 leverage years of experience in developing lung-selective medicines to treat respiratory disease. We are pleased to have received expedited approval of TD-0903's CTA and are working to progress this potential treatment option through clinical trials as quickly as possible," said Rick E Winningham, Chief Executive Officer. "The clinical site that we are working with has a long history of evaluating our inhaled medicines, and we are proud to be working with them to advance TD-0903 into clinical testing."

"There is accumulating evidence that a subgroup of patients with COVID-19 develop a dysfunctional immune response resulting in a cytokine storm within the lungs. JAK inhibition could be an important intervention to treat this hyperinflammation," said Brett Haumann, M.D., Chief Medical Officer. "TD-0903 has been shown in preclinical studies to have broad pan-JAK inhibition, reducing the signaling of multiple cytokines that have been associated with cytokine storm syndrome. Additionally, the nebulized formulation and organ-selective properties of TD-0903 have the potential to address hyperinflammation in the lung without suppressing the systemic immune system, leading to potential patient benefit and improved utilization of limited hospital critical care resources."

About TD-0903

TD-0903 is a lung-selective, nebulized pan-JAK inhibitor that was discovered and developed at Theravance Biopharma. TD-0903 has been shown in experimental murine models to have potent, broad inhibition of JAK-STAT signaling in the airways following challenges with multiple cytokines. By its mechanism, TD-0903 has the potential to block release of cytokines and chemokines that may be associated with acute lung injury and the initiation of a cytokine storm syndrome. Preclinical studies suggest that TD-0903 has a very high lung:plasma ratio and rapid metabolic clearance resulting in low systemic exposure, compatible with its lung selectivity. TD-0903 is administered via nebulized inhalation solution, which further enhances its lung selectivity. Preclinical pharmacodynamic studies indicate that TD-0903 has an extended duration of action that should enable once or twice daily dosing in humans.

As disclosed initially at Theravance Biopharma's December 2018 Research and Development Day, the Company indicated the initial clinical application of TD-0903 would be to explore its utility in preventing/delaying graft rejection among individuals receiving lung transplantation. Although this is still a potential clinical application for TD-0903, in response to the current COVID-19 pandemic, the Company has prioritized activities toward assessing the potential for TD-0903 to treat hospitalized COVID-19 patients who become short of breath and whose blood oxygen levels begin to drop. These patients appear to be at increased risk of respiratory complications including ALI and ARDS. They may also require prolonged hospitalization, continuous oxygen and, in the most severe cases, admission to ICU to assist their breathing with non-invasive and/or mechanical ventilation. Treatment with JAK inhibition is recognized as an important anti-inflammatory mechanism to potentially reduce the hyperinflammation seen in hospitalized COVID-19 patients who develop ALI and ARDS.[1]

Following the completion of the Phase 1 study, Phase 2 will consist of two parts. The first part will assess the safety, tolerability and clinical response to treatment in sequential ascending dose cohorts of COVID-19 patients in the UK. This part of the study will not be formally powered for efficacy but will inform the selection of dose(s) for the second part. The second part of the Phase 2 study will be a larger, multi-center study conducted at hospital-based clinical sites in the UK, and potentially other clinical sites in the European Union and United States. Both of the latter territories would join the Phase 2 study program following review and approval of the relevant regulatory filings required by the relevant EU National Competent Authorities and Food and Drug Administration (FDA). Further details on the program, including more on the Phase 2 study will be provided once these studies have been approved by the appropriate regulatory and ethics review authorities.

For more information please visit: https://investor.theravance.com/events-and-presentations

About the Inhaled JAK Inhibitor Program

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. Limiting JAK inhibition to the lung is expected to improve therapeutic index relative to systemic inhibition. Thus, inhaled JAK inhibitors with lung-restricted exposure are of high interest as potential treatments for respiratory illness.

TD-8236 is the Company's most advanced investigational pan-Janus kinase (JAK) inhibitor currently designed for delivery to the lungs using a dry powder inhaler (DPI). Similar to TD-0903, TD-8236 is a lung-selective agent designed to inhibit the JAK family of enzymes in lung tissue with limited systemic exposure. An extensive set of preclinical pharmacological studies and toxicological studies support its current clinical development in the primary indication of moderate to severe asthma. Insights from the ongoing clinical development of TD-8236 DPI are informing the Company's confidence to bring TD-0903 forward for the treatment of COVID-19 acute lung injury.

In addition, Theravance Biopharma is currently assessing the impact of the COVID-19 pandemic on its operations, including on the commercial operations associated with YUPELRI® (revefenacin inhalation solution) and on the conduct of its clinical development programs for TD-1473, ampreloxetine and TD-8236. The situation continues to evolve as the pandemic's effects are felt around the world. The Company has implemented a comprehensive business continuity plan to support its performance, and it remains well capitalized to advance the company despite the obstacles presented by the current environment. The Company will provide further program updates during its Q1 financial results and business update call in early May 2020.

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.

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, particularly TD-0903, the Company's expectations for product candidates through development and potential regulatory approval and commercialization (including their potential as components of combination therapies), expectations for the repayment of its notes and the expected future commercial performance of TRELEGY ELLIPTA. 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 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: impacts of the COVID-19 global pandemic on our business, 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, risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate technical expertise and supporting infrastructure, 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. Other risks affecting Theravance Biopharma are in the company's Form 10-K filed with the SEC on February 27, 2020, and other periodic reports filed 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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