Theravance Biopharma Responds to COVID-19 Pandemic by Advancing TD-0903 to Treat Hospitalized Patients with Acute Lung Injury

April 9, 2020

- Clinical Trial Application (CTA) submitted in the United Kingdom for first in human study of TD-0903, an investigational lung-selective nebulized JAKi with potential to treat Acute Lung Injury caused by COVID-19

- Near-term clinical development program enables progression from healthy volunteers to hospitalized COVID-19 patients

DUBLIN and SOUTH SAN FRANCISCO, Calif., April 9, 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 it is advancing TD-0903, a lung-selective nebulized Janus kinase inhibitor (JAKi) into clinical development to assess its utility in preventing the cytokine storm associated with Acute Lung Injury (ALI) in patients hospitalized due to COVID-19, with the ultimate goal of preventing progression to Acute Respiratory Distress Syndrome (ARDS).

"In response to the unprecedented healthcare challenges presented by the emergence of COVID-19, we have combined our immunology and respiratory medicine expertise to accelerate development of our nebulized lung-selective JAK inhibitor, TD-0903. With great urgency, we have redirected our program to treat the acute lung injury caused by COVID-19," said Rick E Winningham, Chief Executive Officer. "We recognize how critical it is to help those suffering from shortness of breath and low oxygen levels, including those who need intensive care and ventilation, to address the effects of profound lung hyperinflammation. TD-0903 could provide benefit to hospitalized patients by preventing the progression of lung hyperinflammation and reducing the requirement for, or the duration of, assisted ventilation. As a result, this could improve utilization of limited hospital critical care resources."

"We are pleased to be able to direct our resources and expertise towards helping to treat COVID-19," said Brett Haumann, M.D. Chief Medical Officer. "Janus kinase inhibitors have the potential to inhibit a broad set of immune-modulatory pathways that could prove to be effective in dampening the abnormal immune response that occurs in the lungs of some patients. The nebulized formulation of our lung-selective inhaled JAK inhibitor will allow TD-0903 to be administered directly to the lung in a number of hospitalized settings, including patients who can breathe unaided in the ward, as well as in the ICU setting in patients who require non-invasive or mechanical ventilation. If our initial CTA submission for this study in healthy volunteers is approved and the study is successful, we intend to study TD-0903 in COVID-19 patients in the very near future. We are proud of the tremendous efforts of the global team of Theravance Biopharma scientists and physicians that has enabled us to rapidly progress TD-0903, and we are grateful for their collaboration and dedication to continue its advancement."

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 Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (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]

Upon review and approval of the initial CTA, the Company is planning to initiate a Phase 1 study this month in the United Kingdom (UK), starting with single- and multiple-ascending doses in healthy volunteers to assess safety. Upon regulatory review and approval, the program will then move to a nested Phase 2 study in hospitalized patients with COVID-19. The Phase 2 study 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 European Medicines Authority (EMA) and Food and Drug Administration (FDA). Further details on the program, including more on Phase 1 and Phase 2 studies will be provided once these studies have been approved by the appropriate regulatory and ethics review authorities.

Theravance Biopharma's efforts leverage years of experience in developing lung-selective medicines to treat respiratory disease.

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.

Conference Call and Live Webcast Today at 8:00 a.m. ET

Theravance Biopharma will hold a conference call and live webcast accompanied by slides today at 8:00 a.m. ET (5:00 a.m. PT / 1:00 p.m. GMT). To participate in the live call by telephone, please dial (855) 296-9648 from the U.S., or (920) 663-6266 for international callers and use the confirmation code 5076939. Those interested in listening to the conference call live via the internet may do so by visiting Theravance Biopharma's website at www.theravance.com, under the Investor Relations section, Presentations and Events.

A replay of the conference call will be available on Theravance Biopharma's website for 30 days through May 9, 2020. An audio replay will also be available through 11:00 a.m. ET on April 16, 2020 by dialing (855) 859-2056 from the U.S., or (404) 537-3406 for international callers, and then entering confirmation code 5076939.

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.

THERAVANCE® and the Cross/Star logo are registered trademarks of the Theravance Biopharma group of companies. YUPELRI® is a United States registered trademark of Mylan Specialty L.P. Trademarks, trade names or service marks of other companies appearing on this press release are the property of their respective owners.

This press release 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 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 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: 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 described under the heading "Risk Factors" and elsewhere in Theravance Biopharma's Form 10-K filed with the Securities and Exchange Commission (SEC) on February 27, 2020, in the Form S-3 filed with the SEC on December 3, 2019 and in the Prospectus Supplement filed with the SEC on February 12, 2020. 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.

Contact Information

Gail B. Cohen
Corporate Communications and Investor Relations
917-214-6603

[1] The Lancet, March 13, 2020, "COVID-19: consider cytokine storm syndromes and immunosuppression" Mehta, McAuley, Brown, Sanchez, Tattersall, Manson, et al.

View original content to download multimedia:http://www.prnewswire.com/news-releases/theravance-biopharma-responds-to-covid-19-pandemic-by-advancing-td-0903-to-treat-hospitalized-patients-with-acute-lung-injury-301038037.html

SOURCE Theravance Biopharma, Inc.