Theravance Biopharma, Inc. Announces Top-line Results from Phase 2b Dose-Finding Induction Study of Izencitinib in Patients with Ulcerative Colitis

August 23, 2021

- Randomized, double-blind, placebo-controlled study did not meet the primary endpoint: change in the total Mayo score at week eight, relative to placebo

- Izencitinib was well-tolerated and safety data were consistent with expectations for this gut-selective pan-JAK inhibitor

- Investor conference call and webcast today at 5 pm ET (2 pm PT)

DUBLIN and SOUTH SAN FRANCISCO, Calif., Aug. 23, 2021 /PRNewswire/ -- Theravance Biopharma, Inc. ("Theravance Biopharma" or the "Company") (NASDAQ: TBPH), a diversified biopharmaceutical company primarily focused on the discovery, development, and commercialization of organ-selective medicines, today announced top-line results from its Phase 2b dose-finding induction study of izencitinib, an orally administered, gut-selective pan-Janus kinase (JAK) inhibitor in development for the treatment of ulcerative colitis.

The study did not meet its primary endpoint of change in the total Mayo score or the key secondary endpoint of clinical remission at week 8, relative to placebo. There was a small dose-dependent increase in clinical response measured by the adapted Mayo score, which was driven by a reduction in rectal bleeding.

At all doses, izencitinib was well-tolerated when administered orally once daily for 8 weeks; adverse event rates were similar among patients receiving izencitinib and placebo. There were no instances of perforation, opportunistic infection, major cardiovascular or thromboembolic event, complicated zoster, or non-melanoma skin cancer in patients receiving izencitinib. There were no notable changes in lab values including creatine phosphokinase and lipids in patients receiving izencitinib relative to placebo. Plasma exposure of izencitinib was low, consistent with expectations for a gut-selective medicine.

The Company plans to present study results at a scientific forum.

"We had high expectations for the Phase 2b study after eight weeks of treatment with izencitinib in ulcerative colitis given the totality and consistency of the broad range of clinical, histologic, and biomarker data we saw in the Phase 1b study with only four weeks of treatment, albeit in a small number of patients. We plan to analyze the data to better understand the findings and the potential for optimization of a gut-selective medicine as a treatment for patients with inflammatory bowel diseases," said Rick E Winningham, Chief Executive Officer, Theravance Biopharma. "We are grateful to all those who participated in this clinical trial and to those who are still participating in the Crohn's Phase 2 study – which we expect to report top-line results in late fourth quarter 2021 or early first quarter 2022."

Regarding current plans, the Company will work to understand the complete results and implications for izencitinib. Forthcoming ulcerative colitis data will include results from the 16-week extended induction portion of the study and the 44-week maintenance study. The Company reiterates timing of the top-line results of the Crohn's Phase 2 study in late fourth quarter 2021 or early first quarter 2022. Based on the ulcerative colitis results, the Company will seek to minimize future expenses associated with the izencitinib program.

Conference Call and Live Webcast Today at 5 pm ET

Theravance Biopharma will hold a conference call and live webcast accompanied by slides today at 5 pm ET / 2 pm PT / 10 pm IST. To participate, please dial (855) 296-9648 from the U.S. or (920) 663-6266 for international callers, using the confirmation code 3198387. Those interested in listening to the conference call live via the internet may do so by visiting Theravance.com, under the Investors section, Events and Presentations.

A replay will be available on Theravance.com under the Investors section for 30 days. An audio replay will be also available through 8:00 p.m. ET on August 30, 2021, by dialing (855) 859-2056 from the U.S., or (404) 537-3406 for international callers, and then entering confirmation code 3198387.

About the Phase 2b Dose-Finding Induction Study

The study was a randomized, double-blind, placebo-controlled, multi-center Phase 2b dose-finding induction study (NCT03758443) for the treatment of adults with moderately-to-severely active ulcerative colitis with the primary endpoint at Week 8 (n=239). The safety and efficacy data of this Phase 2b study were intended to inform induction and maintenance dose regimens for a confirmatory Phase 3 induction study and the ongoing maintenance study.

About Theravance Biopharma and Janssen Strategic Collaboration

Theravance Biopharma and Janssen Biotech, Inc. have a global co-development and commercialization agreement for izencitinib, also known as TD-1473, and other compounds for inflammatory intestinal diseases. Under the terms of the agreement, Theravance Biopharma received an upfront payment of $100 million and is eligible to receive up to an additional $900 million in potential payments, if Janssen elects to remain in the collaboration following the completion of certain Phase 2 activities. In that scenario, Theravance Biopharma and Janssen will jointly develop and commercialize izencitinib in inflammatory intestinal diseases, with the two companies sharing expenses related to a potential Phase 3 program and profits in the U.S.

About 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 immune-mediated diseases such as rheumatoid arthritis, myelofibrosis, and ulcerative colitis. However, these products are known to have adverse effects associated with their systemic exposure.

About Izencitinib

Izencitinib, also known as TD-1473, is an orally administered, once-daily, investigational, internally discovered, high affinity, reversible pan-JAK inhibitor which was designed to be gut selective. The gut-selective design provides izencitinib the potential to distribute throughout the gastrointestinal tract tissues and target inflammation at the site of gastrointestinal disease while limiting its systemic exposure. Theravance Biopharma is focused on utilizing izencitinib for the potential treatment of a range of inflammatory intestinal diseases including ulcerative colitis and Crohn's disease.

About Theravance Biopharma

Theravance Biopharma, Inc. is a diversified biopharmaceutical company primarily focused on the discovery, development and commercialization of organ-selective medicines. Its purpose is to pioneer a new generation of small molecule drugs designed to better meet patient needs. Its research is focused in the areas of inflammation and immunology.

In pursuit of its purpose, Theravance Biopharma applies insights and innovation at each stage of its business and utilizes its internal capabilities and those of partners around the world. The Company applies organ-selective expertise to target disease biologically, to discover and develop medicines that may expand the therapeutic index with the goal of maximizing efficacy and limiting systemic side effects. 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). Its pipeline of internally discovered programs is targeted to address significant patient needs.

Theravance Biopharma has 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.

For more information, please visit www.theravance.com.

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Forward-Looking Statements

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 goals, designs, 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, the Company's expectations regarding its allocation of resources, 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 expenses, excluding share-based compensation and other financial results. 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: disagreements with Innoviva, Inc. and TRC LLC, the uncertainty of arbitration and litigation and the possibility that the results of these proceedings could be adverse to the Company, additional future analysis of the data resulting from our clinical trial(s), 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, ineffective or not differentiated, 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. In addition, while we expect the effects of COVID-19 to continue to adversely impact our business operations and financial results, the extent of the impact on our ability to generate revenue from YUPELRI® (revefenacin), our clinical development programs (including but not limited to our later stage clinical programs for izencitinib and ampreloxetine), and the value of and market for our ordinary shares, will depend on future developments that are highly uncertain and cannot be predicted with confidence at this time. These potential future developments include, but are not limited to, the ultimate duration of the COVID-19 pandemic, travel restrictions, quarantines, social distancing and business closure requirements in the United States and in other countries, other measures taken by us and those we work with to help protect individuals from contracting COVID-19, and the effectiveness of actions taken globally to contain and treat the disease, including vaccine availability, distribution, acceptance and effectiveness. Other risks affecting Theravance Biopharma are in the Company's Form 10-Q filed with the SEC on August 5, 2021 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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