Theravance Biopharma Announces Peer-Reviewed Publication Highlighting TD-1473 Program in the Journal of Crohn's and Colitis

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Manuscript Provides Comprehensive Summary of Positive Results from Clinical and Preclinical TD-1473 Studies Conducted to Date

Gut-Selective Pan-JAK Inhibition with TD-1473 Has Demonstrated Minimal Systemic Drug Exposure, Local Target Engagement and Trends Toward Reduced Markers of Ulcerative Colitis Disease Activity

DUBLIN, April 20, 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 the publication of a peer-reviewed paper summarizing positive results from completed Phase 1 clinical and preclinical studies of TD-1473, the Company's gut-selective pan-Janus kinase (JAK) inhibitor. The manuscript, which was published in the *Journal of Crohn's and Colitis*, highlights a broad collection of data demonstrating minimal systemic drug exposure, local target engagement, and trends toward reduced markers of ulcerative colitis disease activity following TD-1473 administration versus placebo.

TD-1473 is a novel, gut-selective oral pan-JAK inhibitor in clinical development with the potential to treat a range of inflammatory intestinal diseases, including ulcerative colitis and Crohn's disease. In contrast to other oral JAK inhibitors under development for inflammatory bowel disease, TD-1473 is gut-selective -- specifically designed to act locally at the site of inflammation in the intestinal wall with limited systemic exposure. TD-1473, which is the focus of a global co-development and commercialization agreement with Janssen Biotech, Inc., is currently being evaluated in a Phase 2b/3 study in ulcerative colitis patients (RHEA) and a Phase 2 study in patients with Crohn's disease (DIONE).

The published manuscript, authored by *William Sandborn*, MD, chief of the division of gastroenterology of University of California, San Diego Health, is titled "Development of gut-selective pan-Janus kinase inhibitor TD-1473 for ulcerative colitis: A translational medicine program." Key study findings featured in the paper, which highlight potential differentiation for TD-1473 as compared to systemically active JAK inhibitors, include:

Phase 1b Clinical Study Results for TD-1473 (40 patients):

- Signals of clinical, histologic and biomarker activity following four weeks of treatment versus placebo, suggesting achievement of localized target engagement in patients with moderately-to-severely active ulcerative colitis
- Minimal systemic exposures and no evidence of systemic immunosuppression or systemic opportunistic infections

Phase 1 Clinical Study Results for TD-1473 (72 subjects):

- Generally well tolerated in healthy subjects as a single dose (up to 1000 mg) and as a daily dose (up to 300 mg) given for 14 days
- Low plasma exposure and high stool concentrations at a range of doses, supporting gut-selective properties

Preclinical Study Results for TD-1473:

- Demonstrated potent inhibition of JAK inflammatory activity
- Gut selectivity, as evidenced by high drug concentrations in colon with minimal plasma drug exposure
- Efficacy in a colitis mouse model, as evidenced by significantly reduced colitis manifestations

"This manuscript offers the most comprehensive collection of data from our ongoing TD-1473 program to date, highlighting the potentially transformational nature of our organ-selective JAK inhibition approach in treating inflammatory intestinal diseases such as ulcerative colitis and Crohn's disease. This compilation of data from preclinical and clinical studies paints a consistent and encouraging picture of TD-1473 in the areas of minimized systemic exposure, localized target engagement and potential to reduce disease activity," said Brett Haumann, MD, chief medical officer at Theravance Biopharma. "Importantly, the content of this manuscript highlights the critical advantages that TD-1473's gut-selective JAK inhibition may offer as compared to systemically active JAK inhibitors, which continue to be associated with dose-limiting side effects that prevent their use at doses that optimize efficacy. We continue to explore the therapeutic potential of TD-1473, including the specific benefits of its gut-selective activity, in our ongoing Phase 2 and 3 studies and look forward to the new findings those trials generate."

The peer-reviewed manuscript in the *Journal of Crohn's and Colitis* can be accessed at: https://doi.org/10.1093/ecco-jcc/jjaa049

About Theravance Biopharma and Janssen Strategic Collaboration

Theravance Biopharma and Janssen Biotech, Inc. have a global co-development and commercialization agreement for TD-1473 and related back-up compounds for inflammatory intestinal diseases, including ulcerative colitis and Crohn's disease. 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. Theravance Biopharma together with Janssen will jointly develop and commercialize TD-1473 in inflammatory intestinal diseases, with the two companies sharing profits in the US and expenses related to a potential Phase 3 program.

About Gut-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, myelofibrosis, and ulcerative colitis. However, these products are known to have side effects associated with their systemic exposure.

TD-1473 is an internally-discovered JAK inhibitor that has demonstrated a high affinity for each of the JAK family of enzymes. Importantly, TD-1473 is a gut-selective treatment specifically designed to distribute adequately and predominantly to the tissues of the intestinal tract, 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 inflammatory intestinal diseases including ulcerative colitis and Crohn's disease, which affect roughly 900,000 and 700,000 patients in the United States, respectively.

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 characteristics, benefits and mechanisms of action of the Company's product and product candidates, and the Company's expectations for product candidates through development and potential regulatory approval and commercialization (including their potential as components of combination therapies and their differentiation from other products or potential products). 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 (including when our product candidates or products 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, 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 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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