Theravance Biopharma Reports Data from TD-1473 Phase 1b Four-Week Study in Oral Late-Breaker Presentation at UEG Week 2018

October 22, 2018

Presented Data Demonstrated Signals of Clinical and Biomarker Activity Suggesting Localized Target Engagement following Four Weeks of Treatment in Patients with Moderately to Severely Active Ulcerative Colitis

Additional Findings Highlight Minimal Systemic Exposure and No Evidence of Systemic Immunosuppression or Infections following TD-1473 Treatment

DUBLIN, Oct. 22, 2018 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company") today reported the results from the exploratory Phase 1b study of the gut-selective pan-Janus kinase (JAK) inhibitor TD-1473 in an oral presentation as part of the late-breaker session at United European Gastroenterology (UEG) Week 2018. Presented data demonstrated that four weeks of TD-1473 treatment led to signals of biological activity and localized target engagement with low systemic exposures and no evidence of systemic immunosuppression or opportunistic infections in patients with moderately to severely active ulcerative colitis. UEG Week 2018 is being held October 20-24, 2018, in Vienna, Austria.

The Phase 1b exploratory study was designed to evaluate the safety, tolerability, and pharmacokinetics (PK) of TD-1473 over a 28-day treatment period. In addition, the study incorporated biomarker analysis and clinical, endoscopic, and histologic assessments as exploratory endpoints to evaluate biological effect. The trial enrolled 40 patients across four treatment arms: placebo (n=9); TD-1473 20 mg/daily (n=10); TD-1473 80 mg/daily (n=10); and, TD-1473 270 mg/daily (n=11).

Study results presented at UEG Week 2018 include:

Clinical Response Rate:

- Trends were observed for higher rates of clinical response for TD-1473 after four weeks of treatment as compared to placebo. Clinical response, which was defined as a reduction in total Mayo score of ≥ 3 points and ≥ 30%, with a reduction in rectal bleeding subscore by ≥ 1 point or an absolute rectal bleeding subscore of ≤ 1 point, was achieved by 2 of 10 patients (20%) in the 20 mg cohort, 2 of 10 patients (20%) in the 80 mg cohort, and 6 of 11 patients (55%) in the 270 mg cohort, compared to 1 of 9 patients (11%) in placebo group.

Endoscopy Improvement: ≥ 1-point reduction in Mayo endoscopic subscore[1] (assessed by central reading):

- Trends were observed for higher rates of endoscopy improvement for TD-1473 after four weeks of treatment as compared to placebo. A ≥ 1-point reduction in Mayo endoscopic subscore was achieved by 2 of 10 patients (20%) in the 20 mg cohort, 3 of 10 patients (30%) in the 80 mg cohort, and 2 of 11 patients (18%) in the 270 mg cohort, compared to 0 of 9 patients (0%) in placebo group.

Evidence of Mucosal Healing:

- Trends were observed for higher rates of mucosal healing for TD-1473 after four weeks of treatment as compared to placebo. Mucosal healing, categorized as having an endoscopic subscore ≤ 1, was achieved by 2 of 10 patients (20%) in the 20 mg cohort, 2 of 10 patients (20%) in the 80 mg cohort, and 1 of 11 patients (9%) in the 270 mg cohort, compared to 0 of 9 patients (0%) in placebo group.

Rectal Bleeding Improvement: ≥ 1-point reduction in Mayo rectal bleeding subscore[1]:

- Trends were observed for higher rates of improvement in rectal bleeding for TD-1473 in the 80 mg and 270 mg cohorts after four weeks of treatment as compared to placebo. A ≥ 1-point reduction in Mayo rectal bleeding subscore was achieved by 3 of 10 patients (30%) in the 20 mg cohort, 7 of 10 patients (70%) in the 80 mg cohort, and 8 of 11 patients (73%) in the 270 mg cohort, compared to 4 of 9 patients (44%) in placebo group.

Surrogate Inflammatory Biomarkers:

- Placebo-adjusted reductions in serum C-reactive protein (CRP) were seen in all TD-1473 cohorts, ranging from 57% to 70%.
- Placebo-adjusted reductions in fecal calprotectin (FC) were seen in the 80 mg and 270 mg cohorts, ranging from 26% to 31%.

Evidence of Gut-Selective Activity:

- Minimal systemic exposure to TD-1473 based on evaluation of plasma levels, consistent with data seen in a previously conducted Phase 1 study of healthy volunteers.
- Colonic tissue concentrations of TD-1473 were higher than plasma at respective dose levels and at or above those required for localized JAK inhibition at the site of inflammation in the 80 mg and 270 mg cohorts.
- No evidence of systemic immunosuppression, and no alterations in total leukocytes, neutrophils, or lymphocytes in patients receiving TD-1473, relative to patients receiving placebo.

Safety and Tolerability:

- TD-1473 was generally well tolerated in the study with no adverse events leading to study drug interruption or discontinuation. There were two serious adverse events (20 mg and 80 mg) which were characterized as hospitalizations for UC exacerbations. There were no serious infections, tuberculosis or other opportunistic infections, bowel perforations, or herpes zoster. Additionally, there were no meaningful changes in hepatic, renal or hematologic laboratory parameters. While high-density lipoprotein (HDL) showed dose-dependent increases from baseline (possibly related to reduced inflammation), there was no evidence of elevated low-density lipoprotein (LDL) relative to placebo or baseline.

"It is very promising to see such clinical and biomarker improvements in ulcerative colitis patients over a short duration of therapy as seen in this Phase 1 study. While the small size of this trial did not allow for these results to achieve statistical significance, the observed trends are very encouraging, particularly with minimal systemic exposure of TD-1473 found at all doses," said Julian Panés, M.D., Chief of the Inflammatory Bowel Disease Unit at Hospital Clínic of Barcelona, Professor of Medicine at Barcelona University and the lead author of the UEG Week presentation. "The findings of this study suggest a unique profile for TD-1473, potentially positioning the compound to offer an elegant approach to harnessing the therapeutic benefits of JAK inhibition, while minimizing adverse events associated with systemic JAK exposure."

TD-1473 is a novel, potent, orally administered and gut-selective 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 specifically designed to act locally at the site of inflammation in the intestinal wall thereby limiting systemic exposure.

Theravance Biopharma is advancing the TD-1473 program into a Phase 2 clinical trial in patients with moderately to severely active Crohn's disease, as well as a Phase 2b/3 induction and maintenance study in ulcerative colitis.

About Theravance Biopharma and Janssen Strategic Collaboration

Theravance Biopharma and Janssen Biotech Inc. and their respective affiliates have established 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 is eligible to receive up to $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 and myelofibrosis, and have demonstrated therapeutic benefit for patients with 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 an oral, 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 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.

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, the Company's expectations for product candidates through development, potential regulatory approval and commercialization (including their potential as components of combination therapies), product sales and the Company's expectations for its 2018 operating loss, excluding share-based compensation. 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: 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, 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. 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 August 2, 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.

References:

[1] Gastroenterology Vol. 148, No. 1, pages 37-51. "Converging Goals of Treatment of Inflammatory Bowel Disease From Clinical Trials and Practice." Barrett G. Levesque, William J. Sandborn, Joannie Ruel, Brian G. Feagan, Bruce E. Sands, and Jean-Frederic Colombel. http://www.gastrojournal.org/article/S0016-5085(14)00999-8/pdf Published online August 12, 2014. Mayo Clinic Score (MCS) as referenced herein, with endoscopic subscore modified such that mild friability is scored as a 2 rather than a 1 (pages 39-40). Clinical response for partial MCS consistent with clinical response for MCS, except criteria for clinical response by partial MCS include a decrease in partial MCS of at least 2 points versus 3 points in the MCS criteria.

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