Theravance Biopharma Announces First Patient Dosed in Registrational Phase 3 Study of Ampreloxetine (TD-9855) for the Treatment of Symptomatic Neurogenic Orthostatic Hypotension

January 28, 2019

Study to evaluate novel, once-daily ampreloxetine in symptomatic nOH patients with primary autonomic failure, including multiple system atrophy, Parkinson's disease, and pure autonomic failure

DUBLIN, Jan. 28, 2019 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company") today announced dosing of the first patient in a registrational Phase 3 clinical trial of ampreloxetine (TD-9855) in patients with symptomatic neurogenic orthostatic hypotension (nOH). Ampreloxetine is an investigational, once-daily norepinephrine reuptake inhibitor (NRI) in development for the treatment of patients with symptomatic nOH.

The Phase 3 study is a four-week, multi-center, randomized, double-blind, placebo-controlled, parallel-group study designed to evaluate the efficacy, safety and tolerability of ampreloxetine in approximately 188 patients with symptomatic nOH caused by primary autonomic failure associated with multiple system atrophy (MSA), Parkinson's disease (PD) and pure autonomic failure (PAF). Patients will be randomized to receive a single 10 mg dose of ampreloxetine or placebo once daily for four weeks. The primary endpoint of the study is change from baseline in dizziness severity, as measured by Orthostatic Hypotension Symptom Assessment (OHSA) Question #1 (OHSA #1, a measure of dizziness, lightheadedness or the sensation of being about to black out) at four weeks for ampreloxetine as compared to placebo. The study will evaluate additional efficacy assessments, as well as safety and tolerability measures.

"Given the limitations of currently available therapeutic options, we recognize a significant opportunity exists for a potentially safe and durable treatment for nOH. Positive four-week results achieved in our Phase 2 study provide the basis for advancing ampreloxetine into this registrational Phase 3 program," said Brett Haumann, MD, chief medical officer at Theravance Biopharma. "We are pleased to begin 2019 with this milestone, and in the near term we also anticipate dosing the first patient in the Phase 2b/3 study of TD-1473, our gut-selective JAK inhibitor, in patients with ulcerative colitis."

Theravance Biopharma previously announced positive four-week results from a Phase 2 clinical trial of ampreloxetine in patients with nOH. Findings showed that a majority of patients enrolled in the study's single ascending dose portion demonstrated durable improvements in nOH symptom severity as measured by OHSA #1. Patients treated in the extension phase of the study showed a mean symptom improvement of 2.4 points at four weeks. Importantly, mean symptom improvement was greatest (3.8 points) in nOH patients who reported dizziness symptoms (OHSA #1 $\geq$ 4) at baseline, a pre-defined regulatory and clinical threshold that will be used to enroll patients in Phase 3. Additionally, ampreloxetine consistently increased systolic blood pressure (SBP), including clinically meaningful increases in standing SBP at the three-minute assessment at all time points on all weekly clinic visits. There were no drug-related serious adverse events reported, and ampreloxetine was generally well tolerated in the study.

About nOH

Neurogenic orthostatic hypotension (nOH) is a rare disorder defined as a sustained orthostatic fall in systolic blood pressure (SBP) of ≥ 20 mm Hg or diastolic blood pressure (DBP) of ≥ 10 mm Hg within three minutes of standing. Severely affected patients are unable to stand for extended periods of time because of their decrease in blood pressure, leading to cerebral hypoperfusion and syncope. A debilitating condition, nOH results in a range of symptoms including dizziness, lightheadedness, fainting, fatigue, blurry vision, weakness, trouble concentrating and head and neck pain. nOH is caused by autonomic nervous system (ANS) malfunction and is associated with several underlying medical conditions including multiple system atrophy (MSA), pure autonomic failure (PAF) and Parkinson's disease (PD).

OHSA #1 is an endpoint which is part of the Orthostatic Hypotension Questionnaire, a validated scale assessing the presence of a range of hypotension-related symptoms including dizziness, weakness, problems with vision, fatigue, trouble concentrating and head/neck discomfort. It is based on a scale from 0 (no symptoms) to 10 (worst possible severity of a symptom), with reductions in OHSA points indicating symptom improvement and increases in OHSA score indicating symptom worsening. OHSA #1 specifically measures patients' dizziness, lightheadedness, feeling faint, or feeling like they might black out. OHSA #1 has been accepted as a suitable endpoint in the investigation of neurogenic orthostatic hypotension by FDA.

About Ampreloxetine (TD-9855)

Ampreloxetine is an investigational, once-daily norepinephrine reuptake inhibitor (NRI) being developed for the treatment of patients with symptomatic neurogenic orthostatic hypotension (nOH). The compound has high affinity for binding to norepinephrine transporters. By blocking the action of these transporters, ampreloxetine causes an increase in extracellular concentrations of norepinephrine.

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 characteristics, benefits and mechanisms of action of the Company's product and product candidates, 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: 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 November 8, 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.

Contact Information:

Theravance Biopharma
Alexander Dobbin
650-808-4045
investor.relations@theravance.com

Vida Strategic Partners (media)
Tim Brons
646-319-8981
tbrons@vidasp.com

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