Theravance Biopharma Reports Positive Top-Line Four-Week Data from Phase 2 Trial of TD-9855 for the Treatment of Symptomatic Neurogenic Orthostatic Hypotension

August 1, 2018

Durable Improvements in nOH Symptom Severity Observed as Measured by OHSA Question #1
Findings Demonstrate Consistent Increases in Systolic Blood Pressure (SBP), Including Clinically Meaningful Improvements in Standing SBP at All Time Points
Company Plans to Progress TD-9855 into Registrational Phase 3 Program

DUBLIN, Aug. 1, 2018 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma") today announced positive four-week results from a Phase 2 clinical trial of TD-9855, an investigational, once-daily norepinephrine and serotonin reuptake inhibitor (NSRI) in development for the treatment of patients with symptomatic neurogenic orthostatic hypotension (nOH). Top-line results from the study included durable improvements in patients' disease symptom severity after four weeks of treatment with TD-9855, as measured by Orthostatic Hypotension Symptom Assessment Question #1 (OHSA #1). OHSA #1 is a measure of dizziness, lightheadedness, or the sensation of being about to black out. 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 ≥ 4) at baseline, a pre-defined regulatory and clinical threshold that will be used to enroll patients in Phase 3. Additionally, TD-9855 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 TD-9855 was generally well tolerated in the study. Theravance Biopharma has also concluded its discussions with the U.S. Food and Drug Administration (FDA) on the design of a pivotal Phase 3 registrational program and plans to initiate the program in late 2018 or early 2019.

"Demonstrating improvements in dizziness, one of the key nOH symptoms, coupled with sustained blood pressure benefits up to four weeks, provide very encouraging evidence of the important impact TD-9855 can have on patients afflicted with the condition," said Brett Haumann, MD, Chief Medical Officer of Theravance Biopharma. "We believe the durability of effect observed in patients on active therapy may prove to be a differentiating feature for TD-9855, and data collected in this multi-part clinical trial provide us confidence to advance TD-9855 into a pivotal Phase 3 clinical program."

"Durable and meaningful improvements to symptoms and increased blood pressure in patients with nOH, seen with TD-9855 both acutely and over a period of time, are impressive," said Horacio Kaufmann, MD, FAAN, Felicia B. Axelrod Professor of Dysautonomia Research in the Department of Neurology and professor of medicine and pediatrics at NYU School of Medicine. "Despite currently available options, there remains a need for scientific advancement in the treatment of nOH, and I expect there will be significant interest in TD-9855 among neurologists and autonomic specialists based on the therapeutic and tolerability profiles which emerged in this Phase 2 study."

Results from the Multiple-Part Phase 2 Study

Part C (Extension Phase): Mean Reductions in Symptom Severity and Consistent Increases in Systolic Blood Pressure at Four Weeks; Pronounced Benefits in Patients with Symptomatic nOH

- Sixteen of 21 patients enrolled in Part C completed 29 days of treatment. These 16 patients showed a mean reduction of 2.4 points in OHSA #1 at four weeks, with more than 60% showing a reduction ≥ 2 points. Thirteen of these 16 Part C completers entered the trial with OHSA #1 of ≥ 4 (a threshold that will be applied in the registrational studies). These patients reported a mean OHSA #1 reduction of 3.8 points. Theravance Biopharma intends to focus on patients with similar nOH characteristics in the Phase 3 registrational program.
- In Part C, treatment with TD-9855 led to increased SBP for patients at all visits and all time points measured, including clinically meaningful increases in standing SBP (7 mm Hg or greater) at the three-minute assessment on all time points at all visits.
- The most commonly reported adverse event in Part C was urinary tract infection, known to be a frequent observation in patients with nOH because of impaired bladder function. There were four serious adverse events, and none were assessed as drug-related.

Part A: Responses Reported in Majority of Patients Treated

- Of 34 patients enrolled in Part A, 27 patients showed improvements in either blood pressure and/or standing time. For these 27 patients, improvements in standing time compared to baseline at 10 hours were observed following treatment with

TD-9855, suggesting potential benefit for patients with symptomatic nOH. This part of the study suggested that clinical benefit occurred at doses above 5 mg.

Part B: Statistically Significant Improvement in Blood Pressure from Seated to Standing

- In the placebo-controlled Part B, a statistically significant difference of 30 mm Hg (p = 0.011) was observed in standing SBP between the active and placebo arms at the four-hour post-dose time point, and the increase in blood pressure was maintained above baseline through the nine-hour time point. These patients had a lower than normal mean SBP at baseline, consistent with nOH.

Theravance Biopharma intends to present full results at a future medical meeting.

About the Phase 2 Study in nOH

These top-line data were generated in a Phase 2 study of TD-9855 in neurogenic orthostatic hypotension (nOH) which consists of three parts. Part A is a single ascending dose (from 1 mg up to 20 mg based on patient response) designed to evaluate impact on blood pressure and standing time for TD-9855 as compared to placebo. Part B is a double-blind, single dose study designed to evaluate impact on blood pressure and standing time for TD-9855 as compared to placebo. Part B was discontinued when the trial was amended to include Part C, following the enrollment of ten patients in Part B (five on TD-9855; five on placebo). Part C is an open label extension to Part A designed to evaluate improvement in patients' symptoms and impact on blood pressure. Responders in Part A were eligible to enroll in Part C at up to their highest tolerated Part A dose, which included 5 mg, 10 mg and 20 mg. The primary endpoint of the study was measured after four weeks, although patients can continue to receive medication for up to five months.

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 more than a few seconds 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 concentration 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 regulatory agencies.

About TD-9855

TD-9855 is an investigational, once-daily norepinephrine and serotonin reuptake inhibitor (NSRI) being developed for the treatment of patients with symptomatic neurogenic orthostatic hypotension (nOH). The compound has high affinity for binding to norepinephrine and serotonin transporters. By blocking the action of these transporters, TD-9855 causes an increase in extracellular concentrations of norepinephrine and serotonin. The compound is the focus of an ongoing Phase 2 clinical trial, with plans for the initiation of a Phase 3 registrational study in patients with symptomatic nOH planned by the end of 2018.

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, intestinally restricted 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 May 9, 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.

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