Theravance Biopharma to Present New Ampreloxetine Data at the 2023 International Congress of Parkinson's Disease and Movement Disorders

August 28, 2023

DUBLIN, Aug. 28, 2023 /PRNewswire/ -- Theravance Biopharma, Inc. ("Theravance Biopharma" or the "Company") (NASDAQ: TBPH) today announced new ampreloxetine data in neurogenic orthostatic hypotension (nOH) will be presented at the 2023 International Congress of Parkinson's Disease and Movement Disorders (MDS), taking place August 27-31, 2023, in Copenhagen, Denmark.

"The data presented at this meeting continue to support ampreloxetine's potential to deliver a consistent and durable benefit to MSA patients with nOH with a favorable safety and tolerability profile," said Roy Freeman, MBChB, Professor of Neurology, Director, Center for Autonomic and Peripheral Nerve Disorders, Beth Israel Deaconess Medical Center. *"MSA is a rare, debilitating disease and many MSA patients suffer from symptoms related to poor blood pressure control that have a significant impact on their quality of life."*[1]

Data will be presented in a poster session on Monday, August 28, 2023, starting at 1:00 PM Central European Time (7:00 AM EDT / 4:00 AM PDT / 11:00 AM GMT):

Category: Clinical Trials and Therapy in Movement Disorders (non-PD) (non-Dystonia)

- **Freeman R, et al. Abstract 7**

An Analysis of Subgroups of Multiple System Atrophy Patients from Ampreloxetine Phase 3 Trials

- **Borin M, et al. Abstract 3**

A Multiple-dose Thorough QT Study to Evaluate the Effect of Ampreloxetine on Cardiac Repolarization in Healthy Subjects

Findings Presented at the 2023 MDS Congress:

Ampreloxetine demonstrated the following benefits in MSA (multiple system atrophy) patients from studies 0169 [SEQUOIA] and 0170 [REDWOOD]:

- Clinically-meaningful and nominally statistically significant ($p< 0.05$) improvements over placebo were observed in the Orthostatic Hypotension Symptom Assessment (OHSA) composite score [LS mean difference: -1.6 (95% CI: -2.7, -0.5)] and in the overall Orthostatic Hypotension Questionnaire (OHQ) composite score [LS mean difference: -1.2 (95%CI: -2.3, -0.2)] in Study 0170.

- Post-hoc analysis of Study 0170 indicated a consistent benefit of ampreloxetine relative to placebo across MSA subgroups including MSA sub-type (MSA-P and MSA-C), sex, age, time since MSA diagnosis, time since nOH onset, and the global MSA disability scale (UMSARS Part IV). Subgroup benefits of ampreloxetine ranged from 0.5 to 2.2 point improvements relative to placebo across all subgroup categories and were demonstrated on the OHSA and OHQ composite scores.

- Ampreloxetine was well-tolerated with similar adverse event rates compared to placebo during the placebo-controlled periods of both Study 0169 and Study 0170.

In a separate single-center study evaluating ampreloxetine's effects on cardiac repolarization compared to placebo, 72 healthy subjects were enrolled in a randomized, double-blind, placebo-controlled fashion. At therapeutic (10 mg QD) and supratherapeutic (40 mg QD) doses of ampreloxetine, no clinically relevant effect on the Q-Tc interval, a measure of heart rhythm, was observed in this study, further supporting the cardiovascular safety of ampreloxetine.

About Ampreloxetine

Ampreloxetine, an investigational, once-daily norepinephrine reuptake inhibitor in development for the treatment of symptomatic neurogenic orthostatic hypotension (nOH) in patients with multiple system atrophy (MSA). The unique benefits of ampreloxetine treatment reported in MSA patients from Study 0170 included an increase in norepinephrine levels, a favorable impact on blood pressure, clinically meaningful and durable symptom improvement, and no signal for supine hypertension. The company has been granted an orphan drug designation in the US and, if results support it, plans to file an NDA for full approval based on the Phase 3 CYPRESS study.

About CYPRESS (Study 0197), a Phase 3 Study

Study 0197 (NCT05696717) is currently enrolling. This is a registrational Phase 3, multi-center, randomized withdrawal study to evaluate the efficacy and durability of ampreloxetine in participants with MSA and symptomatic nOH after 20 weeks of treatment; the primary endpoint of the study is change in the Orthostatic Hypotension Symptom Assessment (OHSA) composite score. The Study includes four periods: screening, open label (12-week period, participants will receive a single daily 10 mg dose of ampreloxetine), randomized withdrawal (eight-week period, double-blind, placebo-controlled, participants will receive a single daily 10 mg dose of placebo or ampreloxetine), and a long-term treatment extension. Secondary

outcome measures include change from baseline in Orthostatic Hypotension Daily Activity Scale (OHDAS) item 1 (activities that require standing for a short time) and item 3 (activities that require walking for a short time).

About Study 0170, a Phase 3 Study

Study 0170 (NCT03829657) was a 22-week Phase 3 study comprised of a 16-week open-label period and a 6-week double-blind, placebo-controlled, randomized withdrawal period. This study followed study 0169, a Phase 3, four week randomized, double-blind, placebo-controlled, parallel-group study of ampreloxetine in patients with symptomatic nOH. The primary endpoint for Study 0170 of treatment failure at week 6 was defined as a worsening of both Orthostatic Hypotension Symptom Assessment Scale (OHSA) question #1 and Patient Global Impression of Severity (PGI-S) scores by 1.0 point. After Study 0169 did not meet its primary endpoint, the Company took actions to close out the ongoing clinical program including Study 0170. The study was more than 80% enrolled (n=128/154 planned) despite stopping early. The primary endpoint was not statistically significant for the overall population of patients which included patients with Parkinson's disease, pure autonomic failure and MSA (odds ratio=0.6; p-value=0.196). The pre-specified subgroup analysis by disease type suggests the benefit seen in patients receiving ampreloxetine was largely driven by MSA patients (n=40). An odds ratio of 0.28 (95% CI: 0.05, 1.22) was observed in MSA patients indicating a 72% reduction in the odds of treatment failure with ampreloxetine compared to placebo. The benefit to MSA patients was observed in multiple endpoints including OHSA composite, Orthostatic Hypotension Daily Activities Scale (OHDAS) composite, Orthostatic Hypotension Questionnaire (OHQ) composite and OHSA #1 (read more about the data here).

About Multiple System Atrophy (MSA) and Symptomatic Neurogenic Orthostatic Hypotension (nOH)

MSA is a progressive brain disorder that affects movement and balance and disrupts the function of the autonomic nervous system. The autonomic nervous system controls body functions that are mostly involuntary. One of the most frequent autonomic symptoms associated with MSA is a sudden drop in blood pressure upon standing (nOH).[2] There are approximately 50,000 MSA patients in the US[3] and 70-90% of MSA patients experience nOH symptoms.[4] Despite available therapies, many MSA patients remain symptomatic with nOH.

Neurogenic orthostatic hypotension (nOH) is a rare disorder defined as a fall in systolic blood pressure of ⩾20 mm Hg or diastolic blood pressure of ⩾10 mm Hg, within 3 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 concentrating, and head and neck pain.

About Theravance Biopharma

Theravance Biopharma, Inc.'s focus is to deliver *Medicines that Make a Difference*® in people's lives. In pursuit of its purpose, Theravance Biopharma leverages decades of expertise, which has led to the development of FDA-approved YUPELRI® (revefenacin) inhalation solution indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Ampreloxetine, its late-stage investigational norepinephrine reuptake inhibitor in development for symptomatic neurogenic orthostatic hypotension, has the potential to be a first in class therapy effective in treating a constellation of cardinal symptoms in multiple system atrophy patients. The Company is committed to creating/driving shareholder value.

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

Forward-Looking Statements

This press release 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, as amended, 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 Company's expectations for product candidates through development and potential regulatory approval and commercialization (including their differentiation from other products or potential products) and the Company's expectations regarding its allocation of resources and maintenance of expenditures. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of this 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: whether the milestone thresholds can be achieved, 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 or product are unsafe, ineffective or not differentiated, risks of decisions from regulatory authorities that are unfavorable to the Company, 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, ability to retain key personnel, the impact of the Company's recent restructuring actions on its employees, partners and others, the ability of the Company to protect and to enforce its intellectual property rights, volatility and fluctuations in the trading price and volume of the Company's shares, and general economic and market conditions. Other risks affecting the Company are in the Company's Form 10-Q filed with the SEC on August 9, 2023, 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.

[1] Disclosure: Dr. Freeman is a consultant serving as an advisor for drug development and clinical trial design for Theravance Biopharma.

[2] https://medlineplus.gov/genetics/condition/multiple-system-atrophy/

[3] UCSD Neurological Institute (25K-75K, with ~10K new cases per year); NIH National Institute of Neurological Disorders and Stroke (15K-50K).

[4] Delveinsight MSA Market Forecast (2023); Symptoms associated with orthostatic hypotension in pure autonomic failure and multiple systems atrophy, CJ Mathias (1999).

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