Theravance Biopharma and Mylan Report Positive New Data from Multiple Studies of YUPELRI™ (revefenacin) at the 2018 CHEST Annual Meeting

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Additional Analyses of Phase 3 Program Data Highlight Efficacy Advantages for 175 mcg/day of YUPELRI in Key Patient Subgroups, Demonstrate Acceptable Cardiovascular Safety Profile

DUBLIN and HERTFORDSHIRE, England and PITTSBURGH, Oct. 11, 2018 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma") and Mylan N.V. (NASDAQ: MYL) ("Mylan") today announced that positive new data from multiple studies of YUPELRI ™ (revefenacin) inhalation solution were presented at the 2018 CHEST annual meeting, which was held in San Antonio, Texas on October 6-10, 2018. YUPELRI is an investigational long-acting muscarinic antagonist (LAMA) currently under review by the U.S. Food and Drug Administration (FDA) for the treatment of chronic obstructive pulmonary disease (COPD). The Prescription Drug User Fee Act (PDUFA) date for YUPELRI is November 13, 2018. If approved, YUPELRI would be the first and only once-daily, long-acting nebulized bronchodilator for the treatment of COPD. YUPELRI is designed to be compatible with any standard jet nebulizer.

Details from the three CHEST presentations are as follows:

Efficacy in COPD Patients with Suboptimal PIFR – YUPELRI vs. Tiotropium

Researchers presented new data from a randomized, double-blinded study comparing the efficacy of YUPELRI to tiotropium in patients with moderate to very severe COPD and suboptimal peak inspiratory flow rates (PIFR) (< 60 L/min). 207 subjects were enrolled and randomized to receive either YUPELRI (175 mcg once daily) or tiotropium once daily for 28 days. Efficacy assessments included forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC).

In the intent-to-treat population, the YUPELRI group showed improvements in trough FEV_1 and trough FVC on day 29 compared with tiotropium group; however, these differences did not reach statistical significance. In the prespecified analysis of subjects with severe to very severe COPD (FEV_1 < 50% predicted), which represented approximately 80% of the study population, YUPELRI demonstrated statistically significant improvements in trough FEV_1 ($p = 0.025$) and FVC ($p = 0.034$) as compared to tiotropium. No new adverse events (AEs) were noted for either YUPELRI or tiotropium, and there were numerically fewer AEs observed in patients receiving YUPELRI (11.7%) compared to patients receiving tiotropium (37.5%).

"These results are noteworthy as this represents the first head-to-head study conducted between tiotropium dry powder via Handihaler and a nebulized treatment, such as YUPELRI. Furthermore, by focusing on COPD patients with suboptimal PIFR, the study provides important context around a patient group believed to be well positioned to benefit from once-daily, long-acting nebulized therapy," said Donald A. Mahler, M.D., emeritus professor of medicine at the Geisel School of Medicine at Dartmouth College and lead author of the study. "The statistically significant improvements in trough FEV_1 and FVC shown for YUPELRI as compared to tiotropium in the severe to very severe subpopulation of patients with FEV_1 < 50% predicted suggest that these individuals may be best suited for nebulized therapy. Further confirmation incorporating the learnings from this study is recommended."

Efficacy in COPD Patients with Markers of More Severe Disease – Phase 3 Program Data Analysis

Researchers presented prespecified analyses of data from the YUPELRI Phase 3 program, highlighted by the demonstration of efficacy advantages for YUPELRI dosed at 175 mcg once daily compared to YUPELRI dosed at 88 mcg once daily in four subgroups of patients categorized as being at risk of COPD exacerbations based on markers of more severe COPD. The subgroups included patients on concomitant long-acting beta agonists (LABA), patients on inhaled corticosteroids (ICS), elderly patients (aged > 65 years in the 12-week efficacy trials, aged ≥ 65 in the 12-month safety trial) and patients classified as Global Initiative for Chronic Obstructive Lung Disease Category D (GOLD D).

Pooled data from the two replicate 12-week pivotal Phase 3 efficacy trials demonstrated that YUPELRI dosed at 175 mcg once daily produced greater improvements in trough FEV_1 than YUPELRI dosed at 88 mcg once daily in each of the four analyzed subgroups. These efficacy trends favoring the 175 mcg once daily dose in the subgroups are consistent with those reported for the entire intent-to-treat population in the two Phase 3 efficacy trials.

Additionally, data from the 12-month Phase 3 safety trial demonstrated that YUPELRI dosed at 175 mcg once daily produced greater improvements in trough FEV_1 than YUPELRI dosed at 88 mcg once daily in the LABA subgroup. The YUPELRI doses were equally effective at improving trough FEV_1 in the ICS and elderly subgroups in the 12-month safety study.

Cardiovascular Safety: Review of Randomized, Controlled Trial Data, Including Phase 3 Program

Researchers conducted a review of cardiovascular (CV) safety data from four clinical studies of YUPELRI including the two replicate 12-week pivotal Phase 3 efficacy trials, the 12-month Phase 3 safety trial and a Phase 1 QT study in healthy subjects. The data analysis demonstrated that once-daily YUPELRI dosed for up to 52 weeks did not prolong QT interval or increase risk of major adverse cardiac events (MACE). Detailed findings include:

- Single YUPELRI doses of up 700 mcg did not have a clinically meaningful effect on cardiac repolarization (QTcF) in healthy patients.
- In the two Phase 3 efficacy studies in patients with moderate to very severe COPD, incidences of prolonged QTcF interval

(> 450 msec in males, > 470 msec in females) were similar for placebo and YUPELRI dosed at 88 mcg once daily and 175 mcg once daily.
- In the Phase 3 safety trial in patients with moderate to very severe COPD, incidences of prolonged QTcF interval were similar for YUPELRI dosed at 175 mcg once daily and tiotropium, and slightly lower for YUPELRI dosed at 88 mcg once daily.
- There was no observed increased risk of MACE identified for either YUPELRI dose compared to tiotropium or placebo in the three Phase 3 clinical trials. Only one MACE seen in the Phase 3 program was considered possibly/probably related to YUPELRI.

Theravance Biopharma and Mylan previously reported that in two replicate pivotal Phase 3 efficacy studies, YUPELRI demonstrated statistically significant and clinically meaningful improvements as compared to placebo in trough FEV_1 and in overall treatment effect on trough FEV_1 (OTE FEV_1) after 12 weeks of dosing.[1] YUPELRI had comparable rates of AEs to placebo, low rates of serious AEs (SAEs), and no clinically meaningful differences in blood parameters or electrocardiogram (ECG) data, across all treatment groups (active and placebo). As previously reported, the most commonly reported AEs, across both trials and across all treatment groups, were exacerbations, cough, dyspnea and headache. Additionally, the companies completed a 12-month Phase 3 safety study in which no new safety issues were identified. Rates of AEs and SAEs in the study were low and comparable to those seen in the standard of care treatment arm.

Theravance Biopharma and its affiliates have partnered with Mylan and its affiliates on the development and commercialization of nebulized revefenacin products for COPD and other respiratory diseases. The companies are developing YUPELRI as a once-daily, nebulized bronchodilator for the treatment of patients with COPD, to be compatible with any standard jet nebulizer.

About Theravance Biopharma and Mylan Strategic Collaboration

Theravance Biopharma and Mylan N.V. and their respective affiliates have established a strategic collaboration to develop and commercialize nebulized revefenacin products for COPD and other respiratory diseases. Under the terms of the agreement, Theravance Biopharma is leading the US development program for the revefenacin inhalation solution product, with all costs related to the registrational program reimbursed by Mylan up until the approval of the first new drug application, after which costs will be shared. Mylan is responsible for ex-US development and commercialization. Theravance Biopharma is eligible to receive up to $220 million in development and sales milestone payments, as well as a profit-sharing arrangement with Mylan on US sales and double-digit royalties on ex-US sales. Additionally, Theravance Biopharma retains worldwide rights to revefenacin delivered through other dosage forms, such as a metered dose inhaler or dry powder inhaler (MDI/DPI), and the rights to nebulized revefenacin in China.

About COPD

COPD is a growing and devastating disease that is the third leading cause of death in the U.S.[2] Nearly 15.7 million Americans (6.4%) report that they have been diagnosed with COPD and more are believed to be undiagnosed.[3] There were more than 700,000 hospital discharges related to COPD in the U.S. reported in 2010. The costs of managing COPD in the U.S. were estimated to be nearly $50 billion in 2010, including $29.5 billion in direct healthcare expenditures, $8 billion in indirect morbidity costs and $12.4 billion in indirect mortality costs.[3]

About YUPELRI

YUPELRI (revefenacin) inhalation solution is a novel investigational once-daily nebulized LAMA under FDA review for the treatment of moderate to very severe COPD. Market research by Theravance Biopharma indicates approximately 9% of the treated COPD patients in the U.S. use nebulizers for ongoing maintenance therapy.[4] LAMAs are a cornerstone of maintenance therapy for COPD and, if approved, YUPELRI would be the first and only once-daily, long-acting single-agent product for COPD patients who require, or prefer, nebulized therapy. YUPELRI's stability in both metered dose inhaler and dry powder device formulations suggest that this LAMA could also serve as a foundation for novel handheld combination products.

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 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.

About Mylan

Mylan is a global pharmaceutical company committed to setting new standards in healthcare. Working together around the world to provide 7 billion people access to high quality medicine, we innovate to satisfy unmet needs; make reliability and service excellence a habit; do what's right, not what's easy; and impact the future through passionate global leadership. We offer a growing portfolio of more than 7,500 marketed products around the world, including antiretroviral therapies on which more than 40% of people being treated for HIV/AIDS globally depend. We market our products in more than 165 countries and territories. We are one of the world's largest producers of active pharmaceutical ingredients. Every member of our approximately 35,000-strong workforce is dedicated to creating better health for a better world, one person at a time. Learn more at Mylan.com. We routinely post information that may be important to investors on our website at investor.mylan.com.

This press release includes statements that constitute "forward-looking statements", including with regard to: the outcome of clinical studies; that, if approved, YUPELRI would be the first and only once-daily, long-acting nebulized bronchodilator for the treatment of COPD; if approved, YUPELRI would be the first and only once-daily, long-acting single-agent product for COPD patients who require, or prefer, nebulized therapy; and that YUPELRI's stability in both metered dose inhaler and dry powder device formulations, suggest that this LAMA could also serve as a foundation for novel handheld combination products. These statements are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Because such statements inherently involve risks and uncertainties, actual future results may differ materially from those expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to: success of clinical trials and our or our partners' ability to execute on new product opportunities; any regulatory, legal or other impediments to our or our partners' ability to bring products to market; other risks inherent in product development; the scope, timing, and outcome of any ongoing legal proceedings, including government investigations, and the impact of any such proceedings on our or our partners' businesses; actions and decisions of healthcare and pharmaceutical regulators, and changes in healthcare and pharmaceutical laws and regulations, in the United States and abroad; the impact of competition; strategies by competitors or other third parties to delay or prevent product introductions; the effect of any changes in our or our partners' customer and supplier relationships and customer purchasing patterns; any other changes in third-party relationships; changes in the economic and financial conditions of the businesses of Mylan or its partners; uncertainties and matters beyond the control of management; and the other risks detailed in Mylan's filings with the Securities and Exchange Commission. Mylan undertakes no obligation to update these statements for revisions or changes after the date of this release.

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References

[1] "Clinically meaningful" is defined by industry established Minimal Clinically Important Difference (MCID) for lung function (100 mL improvement in FEV1).

[2] American Lung Association. "Chronic Obstructive Pulmonary Disease (COPD)" http://www.lung.org/lung-health-and-diseases/lung-disease-lookup/copd. Accessed on September 29, 2016.

[3] Center for Disease Control, COPD https://www.cdc.gov/copd/index.html. Accessed on January 3, 2018.

[4] TBPH market research (N = 160 physicians); Refers to US COPD patients

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