Theravance Biopharma and Mylan Present Additional YUPELRI® (revefenacin) Phase 3 Data Analysis at the 2019 ATS International Conference

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Post-Hoc Analysis Highlights the Potential Role of YUPELRI in the COPD Treatment Paradigm
Additional Analyses Demonstrate Commitment to Further Scientific Understanding of COPD

DUBLIN and HERTFORDSHIRE, England and PITTSBURGH, May 20, 2019 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma") and Mylan N.V. (NASDAQ: MYL) ("Mylan") today announced the presentation of data from its pivotal Phase 3 efficacy studies and a 52-week safety study at the 2019 American Thoracic Society (ATS) International Conference in Dallas, Texas.

YUPELRI® (revefenacin) inhalation solution, a long-acting muscarinic antagonist (LAMA), is the first and only once-daily, nebulized bronchodilator approved for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in the U.S.

Safety and Efficacy in Concomitant LABA or ICS/LABA Treatment COPD Patient Subgroup

Researchers presented a subgroup analysis of data from the revefenacin Phase 3 program of patients treated concurrently with long-acting beta agonists (LABA) either with or without inhaled corticosteroids (ICS). A prespecified subgroup analysis was conducted on pooled data from two 12-week replicate placebo-controlled trials (n=812). Separately, exploratory endpoint data from a 52-week randomized, tiotropium-controlled safety trial were analyzed (n=670). Overall, an average of 43% of patients across the three studies were using concurrent LABA or LABA/ICS combination therapy. This subgroup had more severe disease at baseline. The results suggest the use of YUPELRI with LABA or ICS/LABA may provide additional COPD symptom control particularly in patients with more severe disease, though additional studies are needed to confirm any such benefit. In the analysis of the pooled data (studies 126 and 127), the once daily nebulized treatment with revefenacin produced greater improvements from baseline compared with placebo ($p < 0.0001$) in day 85 trough FEV_1 among the non-LABA and LABA subgroups. Additionally, a clinically significant improvement of an approximately 100-mL increase in trough FEV_1 was sustained for 12 weeks for those treated with revefenacin in both the LABA and non-LABA subgroups.

YUPELRI is a long-term maintenance therapy and should not be initiated in patients during acutely deteriorating or potentially life-threatening episodes of COPD, use with caution in patients with narrow-angle glaucoma, and worsening of urinary retention may occur. The most common adverse events in clinical trials included cough, nasopharyngitis, upper respiratory infection, headache and back pain.

"These findings add to the growing body of evidence that YUPELRI may offer meaningful benefits to a broad range of COPD patients, including those with more severe disease," said Sanjay Sethi, M.D., professor and chief of pulmonary, critical care and sleep medicine at the University of Buffalo'sJacobs School of Medicine & Biomedical Sciences and lead author of the study. "As these COPD patients often require combination treatment with both a LAMA and a LABA to manage their disease, these data provide additional information for healthcare providers to consider when treating their COPD patients."

Brett Haumann, M.D., chief medical officer at Theravance Biopharma commented, "These analyses provide further information regarding YUPELRI, which may be relevant to the treatment of patients with COPD, including those on the severe end of the disease spectrum. We believe this provides additional valuable information on the benefits that YUPELRI can offer to patients, particularly for those battling more severe COPD."

Walt Owens, Mylan's head of global biologics and respiratory science and operations, commented, "These data demonstrate our ongoing commitment to address important unmet needs for patients living with COPD through scientific advancement following FDA approval of YUPELRI. We are very pleased with the continued YUPELRI clinical development program and are excited to have the opportunity to highlight these findings at ATS."

The companies also presented the following two posters at ATS that add to the scientific understanding and potential clinical significance of peak inspiratory flow rate (PIFR) measurements in patients with COPD:

Technical Peak Inspiratory Flow Rate (PIFR) Measurement

PIFR may be an important measurement in deciding whether COPD patients are able to gain full benefit from their handheld inhalers or whether they would be better suited to treatment with a nebulized product. Researchers proposed a method for measuring PIFR in clinical trials that optimizes the repeatability of the measurements and also defines a model to characterize the relationship between PIFR measured using different resistances – the resistance in the DISKUS® device compared with the resistance in the HandiHaler® device. Based on an analysis of data from COPD patients with suboptimal PIFR, researchers suggest that at least three measures of PIFR using the In-Check DIAL device are taken until the two highest measurements meet the repeatability limit for the resistance used (10 L/min against $PIFR_D$ and 5 L/min against $PIFR_{HH}$). Researchers propose using the resistance of the dry powder inhaler (DPI) that the patient is using for treatment at the time when measuring PIFR.

Suboptimal PIFR Associated with Greater Dyspnea

Baseline PIFR to DISKUS® resistance ($PIFR_D$) and severity of dyspnea – the medical term for shortness of breath – were analyzed from two clinical studies. Researchers found that patients with suboptimal $PIFR_D$ (<60 L/min) had more severe dyspnea than patients with similar obstruction and optimal $PIFR_D$ (≥60 L/min). According to the researchers, the differences in dyspnea observed may represent the effect of inspiratory limitation seen in

those with suboptimal $PIFR_D$ on their respiratory muscle function, lung hyperinflation or air trapping.

YUPELRI was approved in November 2018 based on data from two replicate pivotal Phase 3 efficacy studies which 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 adverse events (SAEs), and no clinically meaningful differences in blood parameters or electrocardiogram (ECG) data, across all treatment groups (active and placebo). YUPELRI should not be used in acutely deteriorating COPD or to treat acute symptoms. YUPELRI use should be discontinued if paradoxical bronchospasm occurs. As previously reported, the most commonly reported adverse events, across both trials and across all treatment groups, were cough, nasopharyngitis, upper respiratory tract infection, headache, and back pain. Additionally, the companies completed a 12-month Phase 3 open-label safety study versus tiotropium 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 tiotropium 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. YUPELRI is a once-daily, nebulized bronchodilator for the treatment of patients with COPD and is 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 U.S. 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-U.S. 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 U.S. sales and double-digit royalties on ex-U.S. 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 once-daily nebulized LAMA approved for the maintenance treatment of COPD in the U.S. 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 YUPELRI is positioned as a first-in-class once-daily single-agent bronchodilator 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.

Important Safety Information
YUPELRI is contraindicated in patients with hypersensitivity to revefenacin or any component of this product.

YUPELRI should not be initiated in patients during acutely deteriorating or potentially life-threatening episodes of COPD, or for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. Acute symptoms should be treated with an inhaled short-acting $beta_2$-agonist.

As with other inhaled medicines, YUPELRI can produce paradoxical bronchospasm that may be life-threatening. If paradoxical bronchospasm occurs following dosing with YUPELRI, it should be treated immediately with an inhaled, short-acting bronchodilator. YUPELRI should be discontinued immediately and alternative therapy should be instituted.

YUPELRI should be used with caution in patients with narrow-angle glaucoma. Patients should be instructed to immediately consult their healthcare provider if they develop any signs and symptoms of acute narrow-angle glaucoma, including eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal edema.

Worsening of urinary retention may occur. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction and instruct patients to contact a healthcare provider immediately if symptoms occur.

Immediate hypersensitivity reactions may occur after administration of YUPELRI. If a reaction occurs, YUPELRI should be stopped at once and alternative treatments considered.

The most common adverse reactions occurring in clinical trials at an incidence greater than or equal to 2% in the YUPELRI group, and higher than placebo, included cough, nasopharyngitis, upper respiratory infection, headache and back pain.

Coadministration of anticholinergic medicines or OATP1B1 and OATP1B3 inhibitors with YUPELRI is not recommended.

YUPELRI is not recommended in patients with any degree of hepatic impairment.

Please see the full Prescribing Information.

For additional information please contact us at 800-395-3376.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

About Theravance Biopharma

Theravance Biopharma, Inc. ("Theravance Biopharma") is a diversified biopharmaceutical company primarily focused on the discovery, development and commercialization of organ-selective medicines. Our purpose is to create transformational medicines to improve the lives of patients suffering from serious illnesses. Our research is focused in the areas of inflammation and immunology.

In pursuit of our purpose, we apply insights and innovation at each stage of our business and utilize our internal capabilities and those of partners around the world. We apply organ-selective expertise to biologically compelling targets to discover and develop medicines designed to treat underserved localized diseases and to limit systemic exposure, in order to maximize patient benefit and minimize risk. These efforts leverage years of experience in developing lung-selective medicines to treat respiratory disease, including FDA-approved YUPELRITM (revefenacin) inhalation solution indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Our pipeline of internally discovered programs is targeted to address significant patient needs.

We have an economic interest in potential future payments from 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, and 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's Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 10, 2019 and 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 trials. These statements are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Because forward-looking statements inherently involve risks and uncertainties, actual future results may differ materially from those expressed or implied by such statements. Factors that could cause or contribute to such differences include, but are not limited to any changes in, interruptions to, or difficulties with Mylan's or its partners' ability to develop, manufacture, and commercialize products; the effect of any changes in Mylan's or its partners' customer and supplier relationships and customer purchasing patterns; other changes in third-party relationships; the impact of competition; changes in the economic and financial conditions of the businesses of Mylan or its partners; the scope, timing, and outcome of any ongoing legal proceedings and the impact of any such proceedings on Mylan's or its partners' business; any regulatory, legal, or other impediments to Mylan's or its partners' ability to bring products to market; actions and decisions of healthcare and pharmaceutical regulators, and changes in healthcare and pharmaceutical laws and regulations, in the United States and abroad; Mylan's and its partners' ability to protect intellectual property and preserve intellectual property rights; risks associated with international operations; other 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.

References

[1] "Clinically meaningful" is defined by industry established Minimal Clinically Important Difference (MCID) for lung function (100 mL improvement in FEV_1).

[2] American Lung Association. "Chronic Obstructive Pulmonary Disease (COPD)" http://www.lung.org/lung-health-and-diseases/lung-disease-lookup/copd. Accessed on May 13, 2019.

[3] Center for Disease Control, COPD https://www.cdc.gov/copd/index.html. Accessed on May 13, 2019.

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

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3-data-analysis-at-the-2019-ats-international-conference-300852884.html

SOURCE Mylan N.V.; Theravance Biopharma, Inc.

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