Theravance Biopharma and Mylan Announce FDA Acceptance of New Drug Application for Revefenacin (TD-4208) in Adults with Chronic Obstructive Pulmonary Disease

January 29, 2018

FDA Assigns PDUFA Target Action Date of November 13, 2018

DUBLIN and HERTFORDSHIRE, England and PITTSBURGH, Jan. 29, 2018 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma") and Mylan N.V. (NASDAQ, TASE: MYL) ("Mylan") today announced that the U.S. Food and Drug Administration (FDA) has accepted for review the companies' recently submitted New Drug Application (NDA) for revefenacin (TD-4208), an investigational long-acting muscarinic antagonist (LAMA). If approved, revefenacin would be the first once-daily, nebulized bronchodilator for the treatment of chronic obstructive pulmonary disease (COPD). The FDA has assigned a Prescription Drug User Fee Act (PDUFA) target action date of November 13, 2018, and indicated that it does not currently plan to convene an advisory committee meeting to discuss the NDA.

"The acceptance of our NDA moves us closer to providing COPD patients with access to once-daily, nebulized LAMA therapy. With positive results in our Phase 3 program, we believe that revefenacin is well positioned to fill this important need," said Rick E Winningham, chairman and chief executive officer of Theravance Biopharma. "I commend the team at Theravance Biopharma and Mylan for producing a high quality submission, and we look forward to working with the FDA in its review of our application."

"Today, patients with moderate to severe COPD do not have access to a nebulized LAMA as a treatment option yet. We believe revefenacin, when approved, represents an important advancement in respiratory care by offering a convenient once-daily option for patients, and further strengthens Mylan's robust and growing respiratory portfolio," said Mylan President Rajiv Malik. "We are extremely pleased that the revefenacin NDA has been accepted for FDA review, as it demonstrates the success of our collaboration with Theravance Biopharma, our collective expertise in complex products and the quality of the revefenacin development program."

Theravance Biopharma and Mylan previously reported that in two replicate pivotal Phase 3 efficacy studies, revefenacin demonstrated statistically significant and clinically meaningful improvements as compared to placebo in trough forced expiratory volume in one second (FEV1) and in overall treatment effect on trough FEV1 (OTE FEV1) after 12 weeks of dosing.[1] Both doses of revefenacin had comparable rates of adverse events (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). As previously reported, the most commonly reported adverse events, across both trials and across all treatment groups, were exacerbations, cough, dyspnea and headache. Additionally, the companies have previously announced positive results from the 12-month Phase 3 safety study, which did not identify new safety issues. 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 revefenacin as a once-daily, nebulized bronchodilator for the treatment of patients with COPD that will be compatible with a range of jet nebulizers.

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 Revefenacin

Revefenacin (TD-4208) 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, revefenacin has the potential to be a best-in-class once-daily single-agent product for COPD patients who require, or prefer, nebulized therapy. Revefenacin'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 is a diversified biopharmaceutical company with the core purpose of creating medicines that help improve the lives of patients suffering from serious illness.

Our pipeline of internally discovered product candidates includes potential best-in-class medicines to address the unmet needs of patients being treated for serious conditions primarily in the acute care setting. VIBATIV® (telavancin), our first commercial product, is a once-daily dual-mechanism antibiotic approved in the U.S., Europe and certain other countries for certain difficult-to-treat infections. Revefenacin (TD-4208) is a long-acting muscarinic antagonist (LAMA) being developed as a potential once-daily, nebulized treatment for chronic obstructive pulmonary disease (COPD). Our neprilysin (NEP) inhibitor program is designed to develop selective NEP inhibitors for the treatment of a range of major cardiovascular and renal diseases, including acute and chronic heart failure, hypertension and chronic kidney diseases, such as diabetic nephropathy. Our research efforts are focused in the areas of inflammation and immunology, with the goal of designing medicines that provide targeted drug delivery to tissues in the lung and intestinal tract in order to maximize patient benefit and minimize risk. The first program to emerge from this research is designed to develop intestinally restricted pan-Janus kinase (JAK) inhibitors for the treatment of a range of inflammatory intestinal diseases.

In addition, we have an economic interest in future payments that may be made by Glaxo Group Limited or one of its affiliates (GSK) pursuant to its agreements with Innoviva, Inc. relating to certain drug development programs, including Trelegy Ellipta (the combination of fluticasone furoate, umeclidinium, and vilanterol in a single ELLIPTA® inhaler, previously referred to as the Closed Triple), currently approved in the US for the treatment of appropriate COPD patients and in development for the treatment of COPD in several other countries. The product is also currently in development for the treatment of asthma.

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, 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) and the Company's expectations for product sales. 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), the feasibility of undertaking future clinical trials for our product candidates based on FDA policies and feedback, 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 product and product candidates, 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, 2017and 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 target action date; that, if approved, revefenacin would be the first once-daily, nebulized bronchodilator for the treatment of COPD; that the acceptance of the NDA moves us closer to providing COPD patients with access to once-daily, nebulized LAMA therapy; that with positive results in the Phase 3 program, we believe that revefenacin is well positioned to fill this important need. We believe revefenacin, when approved, represents an important advancement in respiratory care by offering a convenient once-daily option for patients, and further strengthens Mylan's robust and growing respiratory portfolio; and that revefenacin's acceptance by FDA demonstrates the success of Mylan's collaboration with Theravance Biopharma, our collective expertise in complex products and the quality of the revefenacin development program. 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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