



October 20, 2016

Theravance Biopharma and Mylan Announce Positive Results from Two Pivotal Phase 3 Studies of Revefenacin (TD-4208) for the Treatment of Chronic Obstructive Pulmonary Disease (COPD)

Revefenacin Meets Primary Efficacy Endpoint and is Shown to be Well-Tolerated in Both Studies; Twelve-Month Safety Trial Ongoing and Targeted for Completion in 2017

DUBLIN and HERTFORDSHIRE, England and PITTSBURGH, Oct. 20, 2016 /PRNewswire/ -- Theravance Biopharma, Inc. ("Theravance Biopharma") and Mylan N.V. (NASDAQ, TASE: MYL) ("Mylan") today announced positive results from two replicate Phase 3 efficacy studies of revefenacin (TD-4208), an investigational long-acting muscarinic antagonist (LAMA) and the first once-daily, nebulized bronchodilator in development for the treatment of chronic obstructive pulmonary disease (COPD). Top-line results across more than 1,250 moderate to very severe COPD patients confirmed that both Phase 3 studies met their primary efficacy endpoint, demonstrating statistically significant improvements over placebo in trough forced expiratory volume in one second (FEV₁) after 12 weeks of dosing for each of the revefenacin doses studied (88 mcg once daily and 175 mcg once daily).



The trials demonstrated statistically and clinically relevant increases in trough FEV₁ after 12 weeks of once-daily dosing. The improvements in trough FEV₁ compared to placebo for the intent-to-treat population across both studies were 118 mL and 145 mL for 88 mcg and 175 mcg, respectively. In pre-specified pooled analyses, revefenacin produced increases in trough FEV₁ in the subgroup (38%) of patients using background long-acting beta agonist (LABA) containing therapies and in the subgroup of patients who were not using concomitant LABA therapy. The improvements in FEV₁ for the LABA subgroup were 92 mL and 135 mL for 88 mcg and 175 mcg, respectively, and for the non-LABA subgroup were 131 mL and 150 mL for 88 mcg and 175 mcg, respectively.

The studies also demonstrated that the 88 mcg and 175 mcg doses of revefenacin were generally well-tolerated, with comparable rates of adverse events and serious adverse events across all treatment groups (active and placebo). The most commonly reported adverse events, across both trials and across all treatment groups were exacerbations, cough, dyspnea and headache. There were no reports of blurred vision, narrow-angle glaucoma or worsening of urinary retention, all of which are commonly reported adverse events for this class of medication, and in addition, reports of dry mouth were < 0.5% in the revefenacin treatment arms.

Theravance Biopharma and Mylan plan to present more detailed data from the two efficacy studies at upcoming scientific conferences.

"We are extremely pleased with the outcome of these pivotal Phase 3 efficacy studies. The impressive improvements in FEV₁ have exceeded our expectations, particularly when one considers that in nearly 40% of the patients we added revefenacin to their existing LABA or LABA/ICS therapy. These data confirm that revefenacin has the potential to offer meaningful benefits to patients with moderate to very severe COPD," said Brett Haumann, MD, Chief Medical Officer at Theravance Biopharma. "As the first once-daily nebulized bronchodilator of any class in late-stage development, combined with its compatibility with any standard jet nebulizer, revefenacin is uniquely positioned to address a key unmet need in the treatment of COPD. We look forward to completing our ongoing Phase 3 safety trial in 2017, with the goal of filing an NDA

by the end of 2017."

Mylan President Rajiv Malik commented, "The positive results from these Phase 3 studies represent another exciting milestone in Mylan's robust global respiratory pipeline. We are very pleased with our collaboration with Theravance Biopharma and their work advancing this important program, and we look forward to continuing to work together to bring this product to market. We believe Mylan's strong experience with nebulized products and experienced salesforce in the respiratory segment, which has been further enhanced through our Meda transaction, will help ensure this product's success if approved."

Revefenacin is being developed as the first once-daily, nebulized bronchodilator for the treatment of patients with COPD and will be compatible with a range of jet nebulizers. The Phase 3 efficacy studies were replicate, randomized, double-blind, placebo-controlled, parallel-group trials designed to provide pivotal efficacy data for once-daily revefenacin over a dosing period of twelve weeks. The replicate studies enrolled a combined total over 1,250 patients in the U.S. across a range of disease severity from moderate to very severe COPD and allowed for the concomitant use of long-acting beta agonist (LABA) and/or long-acting beta agonist/inhaled corticosteroid (LABA/ICS) products in a significant proportion (38%) of the studied population. Study investigators tested two doses (88 mcg and 175 mcg) of revefenacin inhalation solution or matched placebo administered once daily via a standard jet nebulizer in moderate to very severe COPD patients.

In addition to the two efficacy trials, the revefenacin Phase 3 program includes an ongoing twelve-month, open-label, active comparator safety study in more than 1,050 patients, which is expected to be completed in 2017. Together, the three studies enrolled approximately 2,300 patients. Should outcomes from the safety study be supportive, Theravance Biopharma expects to file a new drug application (NDA) for revefenacin with the United States Food and Drug Administration (FDA) by the end of 2017. Theravance Biopharma and its affiliates have partnered with Mylan N.V. and its affiliates on the development and commercialization of nebulized revefenacin products for COPD and other respiratory diseases.

Conference Call Today at 8:00 am ET

Theravance Biopharma will hold a conference call and webcast presentation today at 8:00 am ET to discuss the results of the Phase 3 efficacy studies of revefenacin and provide a brief business update. To participate in the live call by telephone, please dial (855) 296-9648 from the U.S., or (920) 663-6266 for international callers, using the confirmation code 1078310. To listen to the conference call live via the internet please visit Theravance Biopharma's website at www.theravance.com, under the Investor Relations section, Presentations and Events. To listen to the live call please go to Theravance Biopharma's website 15 minutes prior to its start to register, download, and install any necessary audio software.

A replay of the conference call will be available on Theravance Biopharma's website through November 20, 2016. An audio replay will also be available through 8:00 am ET on October 27, 2016 by dialing (855) 859-2056 from the U.S., or (404) 537-3406 for international callers, using the confirmation code 1078310.

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 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.¹ An estimated 12.7 million American adults are diagnosed with COPD and an almost equal number are believed to be undiagnosed.² 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.²

About Revefenacin

Revefenacin (TD-4208) is a novel investigational once-daily nebulized LAMA in Phase 3 development 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.³ 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. The product'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 make a difference in 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. Revedfenacin (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 the Closed Triple (the combination of fluticasone furoate, umeclidinium, and vilanterol), currently in development for the treatment of COPD and asthma.

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

THERAVANCE[®], the Cross/Star logo, MEDICINES THAT MAKE A DIFFERENCE[®] and VIBATIV[®] are registered trademarks of the Theravance Biopharma group of companies. Trademarks, trade names or service marks of other companies appearing on this press release are the property of their respective owners.

This press release contains and the conference call 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 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 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 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 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's Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2016 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 2,700 generic and branded pharmaceuticals, including antiretroviral therapies on which approximately 50% of people being treated for HIV/AIDS worldwide depend. We market our products in more than 165 countries and territories. Our global R&D and manufacturing platform includes more than 50 facilities, and we are one of the world's largest producers of active pharmaceutical ingredients. Every member of our more than 40,000-strong workforce is dedicated to creating better health for a better world, one person at a time. Learn more at mylan.com.

This press release includes statements that constitute "forward-looking statements," including with regard to revefenacin having the potential to offer meaningful benefits to patients with moderate to very severe COPD; revefenacin being uniquely positioned to address a key unmet need in the treatment of COPD; goals and expectations to complete the ongoing Phase 3 safety trial in 2017 and submit an NDA regulatory filing in the U.S. by the end of 2017; and Mylan's belief that its strong experience with nebulized products and experienced salesforce in the respiratory segment will help ensure revefenacin's success if approved. 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 ability to execute on new product opportunities; any regulatory, legal or other impediments to our ability to bring our 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 business; 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 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; 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

¹American Lung Association. "Chronic Obstructive Pulmonary Disease (COPD)" <http://www.lung.org/lung-health-and-diseases/lung-disease-lookup/copd>. Accessed on September 29, 2016..

²American Lung Association. "Trends in COPD (Chronic Bronchitis and Emphysema): Morbidity and Mortality" <http://www.lung.org/assets/documents/research/copd-trend-report.pdf>. Accessed on September 29, 2016.

³TBPH market research (N = 160 physicians); Refers to US COPD patients

Logo - <http://photos.prnewswire.com/prnh/20140423/77793>

To view the original version on PR Newswire, visit:<http://www.prnewswire.com/news-releases/theravance-biopharma-and-mylan-announce-positive-results-from-two-pivotal-phase-3-studies-of-revefenacin-td-4208-for-the-treatment-of-chronic-obstructive-pulmonary-disease-copd-300348277.html>

SOURCE Mylan N.V.

News Provided by Acquire Media