Theravance Announces Publication of YUPELRI® (revefenacin) Area Under the Curve Spirometry Analysis in the International Journal of Chronic Obstructive Pulmonary Disease

October 18, 2024

DUBLIN, Oct. 18, 2024 /PRNewswire/ -- Theravance Biopharma, Inc. ("Theravance Biopharma" or the "Company") (NASDAQ: TBPH) today announced the publication of a sub-study of the pivotal 12-week, randomized, registrational revefenacin Phase 3 trials (Trials 0126 [NCT02459080] and 0127 [NCT02512510]) for YUPELRI, the first and only FDA approved once-daily nebulized long-acting muscarinic antagonist (LAMA), evaluating the area under the curve (AUC) lung function effects in moderate-to-very-severe chronic obstructive pulmonary disease (COPD) patients. These data and analyses, published in the *International Journal of Chronic Obstructive Pulmonary Disease*, reinforce that YUPELRI provides consistent and durable improvements in lung function, as compared with placebo, over a full 24-hours.

"Where previous data showed that revefenacin significantly improved peak and trough FEV_1 at Day 85 compared with placebo in patients with moderate-to-very-severe COPD, this subset post-hoc analysis depicts a more comprehensive view of 24-hour bronchodilation as assessed by examining AUC over multiple time periods," said Dr. Donald A. Mahler, Emeritus Professor of Medicine at Geisel School of Medicine at Dartmouth in Hanover, NH and Pulmonologist and Respiratory Director at Valley Regional Hospital in Claremont, NH. *"It provides additional valuable clinical insight into the duration and consistency of revefenacin over the entire dosing interval."*

Dr. Blake LeMaster, Assistant Professor of Medicine, Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt University Medical Center, commented, *"Importantly, this drug also exhibits a substantial peak response as well as bronchodilation over the initial 2-hour period as exhibited by FEV_1 AUC 0-2H."* He added, *"Clinically meaningful bronchodilation was seen within the first 15 minutes of administration, persisting over the 24-hour duration during which patients underwent serial spirometry. These data demonstrate that revefenacin can provide rapid and prolonged bronchodilation with just a single dose."*

Key Study Findings:

- Analysis of a retrospective, pooled sub-study from Phase 3 Studies 0126 and 0127 demonstrated that revefenacin (n = 50) improved bronchodilation versus placebo (n = 47) in patients with moderate-to-very-severe COPD when assessed by FEV_1 AUC.
- Rapid onset of bronchodilation was observed, with a mean FEV_1 difference of 145 mL achieved at 15 minutes, exceeding the accepted Minimal Clinically Important Difference (MCID) of 100 mL with approximately 97.5% confidence.
- Day 84 bronchodilation improvements were sustained over 24 hours vs. placebo, with mean differences of 282 mL, 220 mL, 205 mL and 212 mL for FEV_1 AUC0–2h, AUC0–12h, AUC12–24h and AUC0–24h, respectively, ($p<0.001$ for all).

Trough FEV_1 is an important endpoint often used in COPD trials and provides the magnitude of lung function benefit at the end of a given dosing interval. FEV_1 AUC measurements provide additional information on the magnitude and consistency of bronchodilation throughout the dosing interval, including both daytime and nighttime effects. As patients depend on the magnitude of sustained bronchodilation to address COPD symptoms, combined use of both trough FEV_1 and FEV_1 AUC may allow for a more comprehensive assessment of bronchodilator efficacy to support clinical decision-making.

About Studies 0126 and 0127

Studies 0126 (placebo, n = 209; 88 mcg revefenacin, n = 212; and 175 mcg revefenacin, n = 198), and 0127 (placebo, n = 208; 88 mcg revefenacin, n = 205; and 175 mcg revefenacin, n = 197) were replicate Phase 3 studies which included adults ≥40 years old with documented moderate-to-very-severe COPD, and a current or past smoking history of ≥10 pack-years. Subjects were randomized 1:1:1 to receive revefenacin 88 mcg, revefenacin 175 mcg, or placebo administered once-daily in the morning by a standard jet nebulizer (PARI LC Sprint) for 12 weeks. The prespecified primary efficacy endpoint was change from baseline in trough FEV_1 on Day 85. Peak FEV_1 on Day 1 was a secondary endpoint and FEV_1 AUC from 0 to 2 hours (FEV_1 AUC0–2h) on Days 1, 15, 29, 57, and 84 was a prespecified exploratory endpoint[1]. While both revefenacin 88 mcg and 175 mcg doses were investigated in these trials, the post hoc analysis reported herein focused only on the 175 mcg dose as this is the dose approved by the FDA[2].

About YUPELRI

YUPELRI® (revefenacin) inhalation solution is the first and only once-daily nebulized long-acting muscarinic antagonist (LAMA) approved for the maintenance treatment of COPD in the U.S. LAMAs are recognized by international COPD treatment guidelines as a cornerstone of maintenance therapy for COPD.

Important Safety Information

What is YUPELRI®?

- YUPELRI is a prescription medicine used to treat chronic obstructive pulmonary disease (COPD), a long-term (chronic) lung disease that includes chronic bronchitis, emphysema, or both.

- It is an anticholinergic medicine which helps the muscles around the airway in your lungs stay relaxed to prevent symptoms such as wheezing, cough, chest tightness, and shortness of breath.
- It is used long-term as 1 vial of YUPELRI, 1 time each day inhaled through your nebulizer to improve symptoms of COPD for better breathing.

Who should not use YUPELRI?

- **Do not use YUPELRI if you** have sudden breathing problems. Always have a rescue inhaler with you.
- **Do not use YUPELRI if you** have had an allergic reaction to revefenacin, or any of the other ingredients in YUPELRI (sodium chloride, citric acid, sodium citrate).
- Do not use in children. It is not known if YUPELRI is safe and effective in children.

Before using YUPELRI, tell your healthcare provider about all your medical conditions, including if you:

- have eye problems such as glaucoma. YUPELRI may make your glaucoma worse.
- have prostate or bladder problems, or problems passing urine. YUPELRI may make these problems worse.
- have liver problems.
- are allergic to any of the ingredients in YUPELRI, or any other medicines.
- are pregnant or planning to become pregnant. It is not known if YUPELRI may harm your unborn baby.
- are breastfeeding. It is not known if the medicine in YUPELRI passes into your breast milk and if it can harm your baby.

Tell your healthcare provider about all the medicines you take including prescription and over-the-counter medicines, vitamins, and herbal supplements. YUPELRI and certain other medicines may interact with each other. This may cause serious side effects.

Especially tell your healthcare provider if you take:

- Other anticholinergics (including tiotropium, ipratropium, aclidinium, umeclidinium, glycopyrrolate)
- Atropine

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist each time you get a new medicine.

What are the possible side effects with YUPELRI?

YUPELRI can cause serious side effects, including:

- **Sudden breathing problems immediately after inhaling your medicine.** If you have sudden breathing problems immediately after inhaling your medicine, stop using YUPELRI and call your healthcare provider right away.
- **New or worsened eye problems including acute narrow-angle glaucoma.** Acute narrow-angle glaucoma can cause permanent loss of vision if not treated. Symptoms may include:
    - Red eyes
    - Blurred vision
    - Seeing halos or bright colors around lights
    - Eye pain or discomfort
    - Nausea or vomiting
- **Urinary retention.** People who take YUPELRI may develop new or worse urinary retention. Symptoms of urinary retention may include:
    - difficulty urinating
    - urinating frequently
    - urination in a weak stream or drips
    - painful urination

If you have any of these symptoms, call your healthcare provider right away before taking another dose.

- **Serious allergic reactions.** Call your healthcare provider or get emergency medical care if you get any of the following symptoms of a serious allergic reaction:
    - rash
    - hives
    - severe itching
    - swelling of your face, mouth, and tongue
    - difficulty breathing or swallowing

If you have any of these symptoms, stop taking YUPELRI, and call your healthcare provider right away before taking another dose.

- **Common side effects of YUPELRI include:**
    - Cough

- Runny nose
- Upper respiratory tract infection
- Headache
- Back pain

Tell your healthcare provider if you get any side effects that bother you or that do not go away. These are not all the possible side effects with YUPELRI. Ask your healthcare provider or pharmacist for more information. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

How should I use YUPELRI?

Read the step by step instructions for using YUPELRI in the FDA-approved Prescribing Information and in the Patient Information Leaflet

- **YUPELRI is only for use with a nebulizer.**
- **Do not** use YUPELRI more often than prescribed.
- **Do not** mix YUPELRI with other medicines in your nebulizer.
- **Do not use other medicines that contain an anticholinergic for any reason.**
- **Do not** stop using YUPELRI, even if you are feeling better, unless your healthcare provider tells you to because your symptoms might get worse.
- Call your healthcare provider or get emergency medical care right away if
    - your breathing problems get worse.
    - you need to use your rescue inhaler medicine more often than usual.
    - your rescue inhaler medicine does not relieve your symptoms.

This summary does not include all the information about YUPELRI and is not meant to take the place of a discussion with your healthcare provider about your treatment.

Please see the full prescribing information and instructions for use at www.yupelri.com

About Theravance Biopharma / Viatris Collaboration

Theravance Biopharma and Viatris Inc. and their respective affiliates have established a strategic collaboration to develop and commercialize nebulized revefenacin products for COPD.

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 once-daily norepinephrine reuptake inhibitor in development for symptomatic neurogenic orthostatic hypotension (nOH) in patients with Multiple System Atrophy (MSA), has the potential to be a first in class therapy effective in treating a constellation of cardinal symptoms in MSA patients. The Company is committed to creating/driving shareholder value.

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

Forward-Looking Statements

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, as amended, and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to: the Company's expectations regarding its future profitability, expenses and uses of cash, the Company's goals, designs, strategies, plans and objectives, future growth of YUPELRI sales, future royalty payments, the ability to provide value to shareholders, the Company's regulatory strategies and timing of clinical studies, possible safety, efficacy or differentiation of our investigational therapy, the status of patent infringement litigation initiated by the Company and its partner against certain generic companies in federal district courts; contingent payments due to the Company from the sale of the Company's TRELEGY ELLIPTA royalty interests to Royalty Pharma, and expectations around the use of OHSA scores as endpoints for clinical trials. 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: factors that could increase the Company's cash requirements or expenses beyond its expectations and any factors that could adversely affect its profitability, whether 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, 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 Theravance Biopharma are in the Company's Form 10-Q filed with the SEC on August 8, 2024, 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.

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[1]Ferguson GT, Feldman G, Pudi KK, et al. Improvements in lung function with nebulized revefenacin in the treatment of patients with moderate to very severe COPD: results from two replicate Phase III clinical trials. Chronic Obstr Pulm Dis Apr. 2019;6(2):154–165. doi:10.15326/jcopdf.6.2.2018.0152

[2] YUPELRI (revefenacin). Package Insert. Theravance Biopharma and Mylan Inc.; 2018.

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