Theravance Biopharma Announces Results from the Phase 4 YUPELRI® PIFR-2 Study in Patients with Severe to Very Severe Chronic Obstructive Pulmonary Disease (COPD)

January 5, 2024

DUBLIN, Jan. 5, 2024 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) today announced results from the Phase 4 PIFR-2 study of YUPELRI® (revefenacin) inhalation solution, the only once-daily, nebulized long-acting muscarinic antagonist (LAMA) approved in the U.S. for maintenance treatment of COPD.

The PIFR-2 study aimed to demonstrate greater improvement in lung function for YUPELRI delivered via standard jet nebulizer compared to Spiriva® (tiotropium) delivered via a dry powder inhaler (Spiriva® HandiHaler®) in adults with severe to very severe COPD and suboptimal peak inspiratory flow rate (PIFR).

- The study did not show a statistically significant difference between YUPELRI and Spiriva HandiHaler on the primary endpoint, change from baseline in trough forced expiratory volume in one second (FEV_1) at Day 85.
- Similar lung function improvement was demonstrated in both arms of the study.
- YUPELRI demonstrated safety and tolerability consistent with its profile in previous clinical studies.

Chief Executive Officer Rick E Winningham said: "While the primary endpoint in the Phase 4 PIFR-2 study was not met, YUPELRI demonstrated an efficacy and safety profile consistent with its performance in other clinical studies. We appreciate the growth opportunities that lie ahead for YUPELRI, which is an important option for COPD maintenance care, and look forward to sharing additional details from PIFR-2 in the future, following additional data analyses."

About the PIFR-2 Study

The Phase 4 PIFR-2 Study (NCT05165485) is a randomized, double-blind, parallel-group study, comparing improvements in lung function in adults with severe to very severe COPD (FEV_1 <50% of predicted) and suboptimal PIFR (<55 L/min) following once-daily treatment over 12 weeks with either YUPELRI (revefenacin) inhalation solution delivered via standard jet nebulizer or Spiriva (tiotropium) delivered via a dry powder inhaler (Spiriva HandiHaler). YUPELRI is approved in the U.S. for the maintenance treatment of patients with COPD; Spiriva HandiHaler is approved in the U.S. for the long-term, once-daily, maintenance treatment of bronchospasm associated with COPD, and for reducing COPD exacerbations.

About YUPELRI®

YUPELRI® (revefenacin) inhalation solution is a 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, regardless of severity of disease. Our market research indicates there is an enduring population of COPD patients in the U.S. that either need or prefer nebulized delivery for maintenance therapy. The stability of revefenacin in both metered dose inhaler and dry powder inhaler ("MDI/DPI") formulations suggests that revefenacin could also serve as a foundation for novel handheld combination products.

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.

How should I use YUPELRI?

Read the step by step instructions for using YUPELRI in the FDA-approved Prescribing Information and at the end of this 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.

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 norepinephrine reuptake inhibitor in development for symptomatic neurogenic orthostatic hypotension, has the potential to be a first in class therapy effective in treating a constellation of cardinal symptoms in multiple system atrophy patients. The Company is committed to creating/driving shareholder value.

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

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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.

Theravance Biopharma 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: future YUPELRI sales and sales growth, timing of additional details from PIFR-2, and the ability to provide value to shareholders, the Company's regulatory strategies and timing of clinical studies, and possible safety, efficacy or differentiation of our investigational therapy. 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: whether the 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, ability to retain key personnel, 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 November 9, 2023, 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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