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Theravance Biopharma Announces First Subject Dosed in Phase 1 Clinical Trial of TD-0714, an Inhibitor of Neprilysin (NEP)

First Clinical Study for Compound From Company's Potential Best-in-Class NEP Inhibitor Development Program; Compound Designed for Broad Use in Major Cardiovascular and Renal Diseases

DUBLIN, IRELAND -- (Marketwired) -- 12/08/15 -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company") today announced dosing of the first subject in a Phase 1 clinical trial of TD-0714, the lead drug candidate in the Company's neprilysin (NEP) inhibitor program. This program is designed to develop best-in-class 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.

TD-0714 is an internally-discovered selective inhibitor of NEP, the enzyme responsible for degradation of natriuretic peptides ANP, BNP and CNP. By inhibiting NEP, TD-0714 elevates the levels of these peptides, which may exert protective cardiac and renal effects including vasodilation, diuresis, natriuresis, reversal of maladaptive changes in heart, blood vessels and kidney, prevention of fibrosis, and prevention of end-organ damage. Theravance Biopharma has specifically designed TD-0714 to possess certain key features, including low renal clearance, the potential to be administered once daily, and the flexibility to be combined with other approved and investigational drugs.

The Phase 1 trial is a randomized, double-blind, placebo-controlled, single-ascending dose study investigating the safety, tolerability, pharmacokinetics, and pharmacodynamics of TD-0714. The single-center study's primary endpoints will be the safety and tolerability of TD-0714 in healthy adults. Key secondary endpoints are designed to assess the potential for once-daily dosing and include an assessment of the pharmacodynamics of TD-0714 and the pharmacokinetic half-life. Investigators will also assess TD-0714's potential for low levels of renal clearance.

"The initiation of this first-in-human clinical trial is the next step in our efforts to develop a best-in-class collection of NEP inhibitors with the flexibility to be combined with a range of other mechanistic classes to potentially deliver enhanced outcomes to patients with a range of cardiovascular and renal diseases. Importantly, our preclinical data presented at the 2015 American Heart Association conference support our belief that several of our NEP inhibitors have attractive biological and pharmacokinetic properties with significant therapeutic potential," said Mathai Mammen, M.D., Ph.D., Senior Vice President, Research and Development of Theravance Biopharma. "We believe TD-0714 is an exciting compound with uniquely designed characteristics. In addition, it is just the first in a series of novel NEP inhibitors that have been created at Theravance Biopharma. We are working aggressively to advance additional compounds from this program into the clinic and look forward to achieving key development milestones with those drug candidates as well."

Results from preclinical studies involving several of Theravance Biopharma's NEP inhibitors were recently presented at the American Heart Association Scientific Sessions 2015. Findings demonstrated that the Company's NEP inhibitors are potent and selective inhibitors of neprilysin and demonstrated sustained levels of target engagement over 24-hours after a single oral dose in rats. Data also demonstrated that the compounds produced robust and long-lasting cardiovascular effects in rats that were equivalent to or greater than sacubitril, the NEP inhibitor component of Entresto™, which was recently approved by the United States Food and Drug Administration (FDA) for the treatment of patients with reduced-ejection fraction chronic heart failure. Additionally, in the preclinical studies Theravance Biopharma's compounds were orally bioavailable and demonstrated levels of renal clearance that were low as compared to sacubitril.

About Neprilysin (NEP) Inhibition

Neprilysin (NEP) is an enzyme that degrades natriuretic peptides. These peptides play a protective role in controlling blood pressure and preventing cardiovascular tissue remodeling. Research suggests that inhibiting NEP may result in clinical benefits for patients, including diuresis, control of blood pressure, and reversing maladaptive changes in the heart and vascular tissue in patients with congestive heart failure. Based on this activity, NEP inhibitors may have the potential to treat a range of major cardiovascular and renal diseases, including acute and chronic heart failure, resistant hypertension and chronic kidney disease. In the United States alone, there are roughly six million patients diagnosed with chronic heart failure and approximately one million acute heart failure patients hospitalized annually. Additionally, there are six million Americans affected by resistant hypertension and 26 million with chronic kidney disease.[1]

About Theravance Biopharma

The mission of Theravance Biopharma (NASDAQ: TBPH) is to create value from a unique and diverse set of assets: an approved product; a development pipeline of late-stage assets; and a productive research platform designed for long-term growth.

Our pipeline of internally discovered product candidates includes potential best-in-class opportunities in underserved markets in the acute care setting, representing multiple opportunities for value creation. VIBATIV® (telavancin), our first commercial product, is a once-daily dual-mechanism antibiotic approved in the US, Europe and certain other countries for certain difficult-to-treat infections. Revefenacin (TD-4208) is an investigational long-acting muscarinic antagonist (LAMA) being developed as a potential once-daily, nebulized treatment for chronic obstructive pulmonary disease (COPD). Axelopran (TD-1211) is an investigational potential once-daily, oral treatment for opioid-induced constipation (OIC). Our earlier-stage clinical assets represent novel approaches for potentially treating diseases of the lung and gastrointestinal tract and infectious disease. In addition, we have an economic interest in future payments that may be made by Glaxo Group Limited or one of its affiliates pursuant to its agreements with Theravance, Inc. relating to certain drug development programs, including the combination of fluticasone furoate, umeclidinium and vilanterol (the "Closed Triple").

With our successful drug discovery and development track record, commercial infrastructure, experienced management team and efficient corporate structure, we believe that we are well positioned to create value for our shareholders and make a difference in the lives of patients.

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 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 and results of clinical studies, the potential benefits and mechanisms of action of the Company's product and product candidates and the Company's expectations for product candidates through development and commercialization. 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 or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's product candidates are unsafe or ineffective, 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 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 expertise and supporting infrastructure. Other risks affecting Theravance Biopharma are described under the heading "Risk Factors" contained in Theravance Biopharma's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 12, 2015. In addition to the risks described above and in Theravance Biopharma's other 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.

References:

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