

## **Theravance Biopharma Reports Positive New Data from Multiple Studies of VIBATIV® (telavancin) at IDWeek™ 2017**

October 9, 2017

**Preliminary Data from TOUR™ Observational Patient Registry Demonstrate Clinical Response Rates with VIBATIV® (telavancin) Treatment Range from 64.9 - 72.6% for Patients with Bone and Joint Infections, Bacteremia and Infective Endocarditis**

**Additional Study Results Demonstrate VIBATIV to be 8-Fold More Potent than Competitor Antibiotics Against Difficult-to-Treat *Staphylococcus aureus* Pathogens including Challenging MRSA and MSSA Isolates**

DUBLIN, Oct. 9, 2017 /PRNewswire/ -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company") today announced that positive new data from multiple studies of VIBATIV® (telavancin) were presented at IDWeek™ 2017, which was held in San Diego, CA on October 4 – 8, 2017. Two presentations were made reporting preliminary new data from the ongoing Telavancin Observational Use Registry (TOUR™) study, which is designed to report how VIBATIV® (telavancin) is being used by healthcare practitioners to treat patients in real-world clinical settings. The presented findings, which focus on data from registry patients with diagnoses of bone and joint infections, bacteremia and/or infective endocarditis, report positive clinical responses for VIBATIV treatment ranging from 64.9% to 72.6% in each of these infection types. Positive clinical response was defined as cure or improvement leading to step-down oral therapy. The Company plans to present additional collections of data from the ongoing TOUR study at appropriate upcoming scientific conferences.



The TOUR findings reported at IDWeek are based on a review of preliminary data collected from the fully enrolled registry of 1,059 patients. The Company expects future TOUR analyses to be updated as additional data become available and the study is completed. Details from the two TOUR-related IDWeek presentations are as follows:

### Bone and Joint Infections in TOUR:

Researchers presented preliminary data reported for 288 patients captured in the TOUR study with bone and joint infections. Of these patients, 70.1% failed treatment with initial antibiotic therapy prior to receiving VIBATIV. A positive clinical response was reported for 72.6% of the patients after receiving VIBATIV, with 8.7% of patients failing to respond to treatment and 10.8% having an indeterminate clinical outcome at end of therapy (EOT) with VIBATIV. Eight percent were non-evaluable due to missing or undocumented outcomes. Among the patients that had an outcome assessment at EOT with VIBATIV (n = 265), 78.9% were cured or improved to step-down therapy and 9.4% failed treatment. Methicillin-resistant *Staphylococcus aureus* (*S. aureus*) or MRSA was the most commonly isolated pathogen responsible for the bone and joint infections at baseline. The median VIBATIV daily dose and duration of treatment were 750 mg and 26 days, respectively, and 75% of patients were treated as outpatients. Of the 288 patients, 58 reported an adverse event, six reported a serious adverse event, and 46 discontinued treatment due to an adverse event. The most commonly occurring adverse event was renal failure (9.0%). Four patients died during the course of the study; clinician review of each of these cases determined that none were related to VIBATIV treatment.

### Bacteremia and/or Infective Endocarditis in TOUR:

Researchers presented preliminary data reported for 151 patients captured in the TOUR study with confirmed cases of bacteremia and/or infective endocarditis. Of these patients, 86.1% failed treatment with initial antibiotic therapy prior to receiving VIBATIV. A positive clinical response was reported for 64.9% of the patients after receiving VIBATIV, with 9.3% of patients failing to respond to treatment, 13.2% having an indeterminate clinical outcome at end of therapy (EOT) and 15.2% considered non-evaluable due to missing or undocumented outcomes. Among the patients that had an outcome assessment at EOT (n = 132), 74.2% were cured or improved to step-down therapy and 10.6% failed treatment. MRSA was the most commonly isolated pathogen responsible for bacteremia and/or infective endocarditis. The median VIBATIV daily dose and duration of treatment were 750 mg and 9 days, respectively, and 80.1% of patients were treated as inpatients. Of the 151 patients, 23 reported an adverse event, 18 reported a serious adverse event, and 15 discontinued treatment due to an adverse event. The most commonly occurring adverse event was renal failure (7.9%). Twenty-one patients died during the course of the study. Researchers deemed VIBATIV treatment was potentially related in two of these cases. Both patients had previously exhibited several predisposing comorbidities including sepsis, chronic renal insufficiency and diabetes.

"Bone and joint infections, bacteremia and infective endocarditis each represent a significant treatment challenge for clinicians in today's healthcare environment. We often see treatment failure against these difficult clinical conditions with first-line antibiotic treatment, which was illustrated by the high rates of VIBATIV use as a second-line treatment. This fact highlights the impressive nature of the clinical response rates that were seen with VIBATIV in these patients," said Charles R Sims, M.D., an infectious disease specialist at Baylor CHI St. Luke's Health, The Woodlands, Texas, and lead author of one of the TOUR presentations at IDWeek. "As a clinician who has relied upon VIBATIV to treat patients with challenging infections, these data match my experience."

### Activity Against Challenging *S. aureus* Isolates:

In addition to data collected as part of the TOUR study, researchers also presented results from a third study evaluating the *in vitro* activity of several antibiotics, including VIBATIV, against more than 15,000 *S. aureus* clinical isolates collected from US medical centers from 2014-2016. 100% of the evaluated isolates, including both MRSA and methicillin-susceptible *S. aureus* (MSSA), were susceptible to VIBATIV as measured by the FDA-approved breakpoint, regardless of their type or resistance profile. VIBATIV possessed greater *in vitro* activity than vancomycin, daptomycin and linezolid demonstrated by minimum inhibitory concentrations (MICs) that were 8-fold lower than for those other antibiotics. MICs are a measure used to express *in vitro* activity of an antibiotic against a pathogen. These *in vitro* potency advantages for VIBATIV were seen against all types of *S. aureus* isolates that were tested, including those subsets classified as MRSA or multidrug-resistant (MDR).

"The VIBATIV potency advantages seen against multidrug-resistant pathogens are particularly important based on the fact that this study also demonstrated that multidrug-resistant MRSA rates have increased over the three years evaluated. This trend further highlights the growing threat of antibiotic resistance and the need for potent antibiotics with rapid bactericidal activity to combat the most challenging pathogens in today's healthcare environment," said Christine Slover, PharmD, Director of Medical Affairs at Theravance Biopharma. "The data presented in this study showing greater *in vitro* potency for VIBATIV compared to several well-known competitor antibiotics are consistent with other research results that we have presented at scientific conferences over the past few years. We believe that these data highlight a critical competitive advantage for VIBATIV in the treatment of *S. aureus* in the product's approved indications, particularly those that are most challenging to treat."

### **About TOUR**

TOUR is a multi-center, observational study that has enrolled 1,059 patients from about 50 sites in the US. As a non-interventional study, all treatment decisions are at the discretion of the patient's healthcare provider. Study patients may have treatment initiated in either hospital-based settings or out-patient infusion sites. In order to qualify for enrollment in TOUR, patients must have received at least one dose of VIBATIV and meet specified inclusion criteria. By broadly collecting and examining real-world data related to VIBATIV treatment patterns, clinical effectiveness and safety outcomes in medical practice, Theravance Biopharma aims to create an expansive knowledge base to guide optimal clinical use and future development of the drug.

Theravance Biopharma believes that results from TOUR may serve several important objectives including:

- Assisting in optimizing use in patients currently being treated with VIBATIV;
- Potentially highlighting subsets of patients that may be most appropriate for treatment with VIBATIV; and
- Illustrating current healthcare practitioner's patterns of VIBATIV use.

### **About VIBATIV®(telavancin)**

VIBATIV® was discovered internally in a research program dedicated to finding new antibiotics for serious infections due to *Staphylococcus aureus*(*S. aureus*) and other Gram-positive bacteria, including MRSA and MSSA. VIBATIV is a once-daily, injectable lipoglycopeptide antibiotic with *in vitro* potency, *in vitro* bactericidal activity within six hours, and penetration into target infection sites. The drug is approved in the U.S. for the treatment of adult patients with hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) caused by susceptible isolates of *S. aureus* when alternative treatments are not suitable. In addition, VIBATIV is approved in the U.S. for the treatment of adult patients with complicated skin & skin structure infections (cSSSI) caused by susceptible isolates of Gram-positive bacteria, including *S. aureus*, both methicillin-susceptible (MSSA) and methicillin-resistant (MRSA) strains. The product labeling also describes the use of VIBATIV in treating patients whose pneumonia or skin infection is complicated by concurrent bacteremia.

The product's proven efficacy against difficult-to-treat Gram-positive infections has been demonstrated in several large, multinational registrational studies, which involved one of the largest cohorts of patients with *S. aureus* infections studied to date. Importantly, these studies demonstrated significantly higher cure rates for VIBATIV as compared to vancomycin in HABP/VABP due to any single Gram-positive pathogen or *S. aureus* with MIC  $\geq 1$   $\mu\text{g/mL}$ . Additionally, there is extensive and well-documented evidence of the drug's *in vitro* potency and *in vivo* activity against a broad collection of Gram-positive bacterial pathogens, including those that are considered difficult-to-treat and multidrug-resistant.

VIBATIV is also approved for marketing in Europe, Canada and Russia. Theravance Biopharma plans to market VIBATIV outside the U.S. through a network of partners. To date, the company has secured partners for VIBATIV in the following geographies – Canada, Middle East, North Africa, Israel, Russia, China and India.

### **VIBATIV®(telavancin) Important Safety Information**

#### **Mortality**

Patients with pre-existing moderate/severe renal impairment (CrCl  $\leq 50$  mL/min) who were treated with VIBATIV® for hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia had increased mortality observed versus vancomycin. Use of VIBATIV in patients with pre-existing moderate/severe renal impairment (CrCl  $\leq 50$  mL/min) should be considered only when the anticipated benefit to the patient outweighs the potential risk.

#### **Nephrotoxicity**

New onset or worsening renal impairment occurred in patients who received VIBATIV. Renal adverse events were more likely to occur in patients with baseline comorbidities known to predispose patients to kidney dysfunction and in patients who received concomitant medications known to affect kidney function. Monitor renal function in all patients receiving VIBATIV prior to initiation of treatment, during treatment, and at the end of therapy. If renal function decreases, the benefit of continuing VIBATIV versus discontinuing and initiating therapy with an alternative agent should be assessed.

#### **Fetal Risk**

Women of childbearing potential should have a serum pregnancy test prior to administration of VIBATIV. Avoid use of VIBATIV during pregnancy unless the potential benefit to the patient outweighs the potential risk to the fetus. Adverse developmental outcomes observed in three animal species

at clinically relevant doses raise concerns about potential adverse developmental outcomes in humans. If not already pregnant, women of childbearing potential should use effective contraception during VIBATIV treatment.

#### Contraindication

Intravenous unfractionated heparin sodium is contraindicated with VIBATIV administration due to artificially prolonged activated partial thromboplastin time (aPTT) test results for up to 18 hours after VIBATIV administration.

VIBATIV is contraindicated in patients with a known hypersensitivity to the drug.

#### Hypersensitivity Reactions

Serious and potentially fatal hypersensitivity reactions, including anaphylactic reactions, may occur after first or subsequent doses. VIBATIV should be used with caution in patients with known hypersensitivity to vancomycin.

#### Geriatric Use

Telavancin is substantially excreted by the kidney, and the risk of adverse reactions may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection in this age group.

#### Infusion Related Reactions

VIBATIV is a lipoglycopeptide antibacterial agent and should be administered over a period of 60 minutes to reduce the risk of infusion-related reactions. Rapid intravenous infusions of the glycopeptide class of antimicrobial agents can cause "Red-man Syndrome" like reactions including: flushing of the upper body, urticaria, pruritus, or rash.

#### QTc Prolongation

Caution is warranted when prescribing VIBATIV to patients taking drugs known to prolong the QT interval. In a study involving healthy volunteers, VIBATIV prolonged the QTc interval. Use of VIBATIV should be avoided in patients with congenital long QT syndrome, known prolongation of the QTc interval, uncompensated heart failure, or severe left ventricular hypertrophy.

#### Most Common Adverse Reactions

The most common adverse reactions (greater than or equal to 10% of patients treated with VIBATIV) were diarrhea, taste disturbance, nausea, vomiting, and foamy urine.

Full Prescribing Information, including Boxed Warning and Medication Guide in the U.S., is available at [www.VIBATIV.com](http://www.VIBATIV.com).

#### **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<sup>®</sup> (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. Revenfenacin (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<sup>®</sup> 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](http://www.theravance.com).

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*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 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, 2017 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.*

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