

## **Theravance Biopharma Reports Positive New Data from Multiple Studies of VIBATIV® (telavancin) at 2018 ECCMID™ Conference**

April 23, 2018

### **Data from TOUR™ Observational Patient Registry Demonstrate Clinical Response Rates with VIBATIV® (telavancin) Treatment Range from 76.5 - 78.8% for Obese and Elderly Patient Subgroups Additional Study Results Demonstrate VIBATIV to Have 8- to 32-Fold Greater in vitro Potency than Competitor Antibiotics Against Difficult-to-Treat Staphylococcus aureus Pathogens including Multidrug-Resistant MRSA**

DUBLIN, April 23, 2018 /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 the 28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID™), which is being held in Madrid, Spain on April 21 – 24, 2018. Two presentations were made reporting new data from the 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 classified as elderly or obese, report positive clinical responses for VIBATIV treatment ranging from 76.5% to 78.8% in these patient subgroups. Positive clinical response was defined as cure or improvement leading to step-down oral therapy.



The TOUR findings reported at ECCMID are based on a review of data collected from the fully enrolled registry of 1,063 patients. The Company expects future TOUR analyses to be updated as additional data become available. Details from the two TOUR-related ECCMID presentations are as follows:

#### Obese Patients in TOUR:

Researchers presented data reported for 507 patients in the TOUR study classified as obese (body mass index  $\geq 30$  kg/m<sup>2</sup>). The infection types reported for these patients included complicated skin & skin structure infections (cSSSIs) (53.6%), bone and joint infections (27.8%), bacteremia and endocarditis (9.9%), and lower respiratory tract infections (5.1%). Of these patients, 72.2% failed treatment with initial antibiotic therapy prior to receiving VIBATIV.

Among the patients who had an outcome assessment at end of therapy (EOT) with VIBATIV (n = 458), 78.8% were cured or improved to step-down therapy, 9.2% failed treatment and 12.0% had an indeterminate clinical outcome. The median VIBATIV daily dose and duration of treatment were 7.3 mg/kg and 11 days, respectively. Of the 507 patients, 82 reported an adverse event. Renal failure, the most commonly occurring adverse event, was reported in 28 of the 507 patients and resolved in the majority of these cases. There were no new safety signals identified in this patient subset.

"Obese patients are an interesting TOUR study subgroup as data show that obesity is a risk factor for developing complicated skin & skin structure infections that are associated with MRSA. Highlighting this increased risk is the fact that more than half of the obese patients in TOUR presented with a complicated skin & skin structure infection," said Adnan Siddiqui, M.D., an infectious disease expert at BJC Christian Northeast Hospital in St Louis and lead author of one of the TOUR presentations at ECCMID. "The nearly 80% positive clinical response rate achieved with VIBATIV therapy in the obese patient subgroup is encouraging, particularly considering more than 70% of obese patients in TOUR received VIBATIV after failing treatment with an initial antibiotic."

#### Elderly Patients in TOUR:

Researchers presented data reported for 312 patients in the TOUR study classified as elderly ( $\geq 65$  years of age). The infection types reported for these patients included cSSSIs (47.4%), bone and joint infections (26.0%), bacteremia and endocarditis (17.3%), and lower respiratory tract infections (9.6%). Of these patients, 67.3% failed treatment with initial antibiotic therapy prior to receiving VIBATIV.

Among the patients that had an outcome assessment at EOT with VIBATIV (n = 289), 76.5% were cured or improved to step-down therapy, 11.8% failed treatment and 11.8% had an indeterminate clinical outcome. The median VIBATIV daily dose and duration of treatment were 8.3 mg/kg and 10 days, respectively. Of the 312 patients, 55 reported an adverse event. Renal failure, the most commonly occurring adverse event, was reported in 25 of the 312 patients and resolved in the majority of these cases. There were no new safety signals identified in this patient subset.

"Due to the chronic comorbidity commonly associated with the elderly population, this group is at an elevated risk of acquiring serious infections such as those reported in the TOUR study. Accordingly, there is significant value in using an antibiotic against challenging infections that is highly effective at either curing elderly patients or improving their condition enough to allow step-down therapy," said Jeremy Storm, an infectious disease expert at Rapid City Medical Center in South Dakota, D.O., and lead author of one of the TOUR presentations at ECCMID. "VIBATIV was able to deliver a positive clinical response rate for more than 75% of these patients against a range of challenging infection types."

### Activity Against Challenging Gram-Positive Clinical 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 24,408 Gram-positive clinical isolates collected from medical centers around the world from 2015-2017. 100% of the evaluated *S. aureus* isolates were susceptible to VIBATIV as measured by the FDA-approved breakpoint, regardless of their type or resistance profile, including those considered to be multidrug-resistant (MDR).

VIBATIV possessed greater *in vitro* activity than vancomycin, daptomycin and linezolid demonstrated by minimum inhibitory concentrations (MICs) that were 8- to 32-fold lower than for those other antibiotics against all the *S. aureus* isolates tested, including MDR MRSA. VIBATIV maintained potent *in vitro* activity against ceftaroline-nonsusceptible *S. aureus*, MDR coagulase-negative staphylococci,  $\beta$ -haemolytic streptococci and *Streptococcus pneumoniae* isolate subsets. MICs are a measure used to express *in vitro* activity of an antibiotic against a pathogen.

"Our ongoing surveillance of active global Gram-positive clinical isolates and the susceptibility of those pathogens to current antibiotic treatments continues to demonstrate that VIBATIV possesses greater *in vitro* potency than several well-known competitor antibiotics," said Christine Slover, PharmD, Director of Medical Affairs at Theravance Biopharma. "We believe that this greater *in vitro* activity, especially against pathogens that are as challenging to treat as MDR MRSA, highlights an important competitive advantage for VIBATIV in the product's approved indications."

### **About TOUR**

TOUR is a multi-center, observational study that has enrolled 1,063 patients from 45 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, 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 vancomycin MIC  $\geq 1$   $\mu$ 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 Canada, Russia and Israel. 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, Inc. ("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.

In our relentless pursuit of this objective, we strive to apply insight and innovation at each stage of our business, including research, development and commercialization, and utilize both internal capabilities and those of partners around the world. Our research efforts are focused in the areas of inflammation and immunology. Our research goal is to design localized medicines that target diseased tissues, without systemic exposure, in order to maximize patient benefit and minimize risk. These efforts leverage years of experience in developing localized medicines for the lungs to treat respiratory disease. The first potential medicine to emerge from our research focus on immunology and localized treatments is an oral, intestinally restricted pan-Janus kinase (JAK) inhibitor, currently in development to treat a range of inflammatory intestinal diseases. Our pipeline of internally discovered product candidates will continue to evolve with the goal of creating transformational medicines to address the significant needs of patients.

In addition, we have an economic interest in future payments that may be made by Glaxo Group or one of its affiliates (GSK) pursuant to its agreements with Innoviva, Inc. relating to certain programs, including Trelegy Ellipta.

For more information, please visit [www.theravance.com](http://www.theravance.com).

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