



## **Theravance Biopharma, Inc. (NASDAQ: TBPH)**

**3Q 2017 Financial Results and Business Update**  
**November 7, 2017**

# Cautionary Statement Regarding Forward-Looking Statements

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Under the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, the company cautions investors that any forward-looking statements or projections made by the company are subject to risks and uncertainties that may cause actual results to differ materially from the forward-looking statements or projections.

Examples of forward-looking statements in this presentation include statements relating to the company's business plans and objectives, including financial and operating results, potential partnering transactions and sales targets, 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 (including their potential as components of combination therapies).

The company's forward-looking statements are based on the estimates and assumptions of management as of the date of this presentation and are subject to risks and uncertainties that may cause the actual results to be materially different than those projected, such as risks related to delays or difficulties in commencing or completing clinical studies, the potential that results from clinical or non-clinical studies indicate product candidates are unsafe or ineffective (including when our product candidates are studied in combination with other compounds), delays or failure to achieve and maintain regulatory approvals for product candidates, risks of collaborating with third parties to discover, develop and commercialize products, risks associated with establishing and maintaining sales, marketing and distribution capabilities.

Other risks affecting the company are described under the heading "Risk Factors" and elsewhere in the company's Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2017, and other periodic reports filed with the SEC.

# Upcoming Milestones

## *Multiple Opportunities for Value Creation*

Program	Milestone	Target
TD-1439 (NEP inhibitor)	Phase 1a SAD/MAD results in healthy volunteers	✓
Revefenacin (TD-4208)	Phase 3 long-term safety results in COPD patients	✓
Velusetrag (TD-5108)	Phase 2b results in Gastroparesis patients	✓
TD-1473 (JAK inhibitor)	Phase 1b results in UC patients, Cohort 1	✓
Trelegy Ellipta (FF/UMEC/VI) <sup>1</sup>	Phase 3 IMPACT study completion	✓
Trelegy Ellipta (FF/UMEC/VI) <sup>1</sup>	Regulatory approval in US for COPD <sup>2</sup>	✓
Revefenacin (TD-4208)	NDA submission in US <sup>3</sup>	2017
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TD-1473 (JAK inhibitor)	Phase 1b results in UC patients, Cohorts 2 and 3	2018
TD-9855 (NSRI)	Phase 2a results in nOH patients	2018
Revefenacin (TD-4208)	Phase 3b study results in COPD patients with low PIFR <sup>4</sup>	2018
Revefenacin (TD-4208)	Potential regulatory approval in US for COPD <sup>3</sup>	2018
VIBATIV® (telavancin)	Patient registry study data (TOUR™)	2018
VIBATIV® (telavancin)	Phase 3 study data in Bacteremia patients	2018 / 2019
Trelegy Ellipta (FF/UMEC/VI) <sup>1</sup>	Phase 3 study completion in Asthma patients	2018

3 <sup>1</sup> Economic interests. Regulatory and clinical milestones as reported by GlaxoSmithKline. Trelegy Ellipta previously referred to as the Closed Triple. FF/UMEC/VI= Fluticasone Furoate/Umeclidinium/Vilanterol. <sup>2</sup> For the treatment of appropriate patients with COPD. <sup>3</sup> Submissions, filings, and approvals are subject to preclinical and clinical data and regulatory interactions. <sup>4</sup> Peak inspiratory flow rate.

# TD-1473: Phase 1b First Cohort Demonstrated Localized Target Engagement and Minimal Systemic Exposure

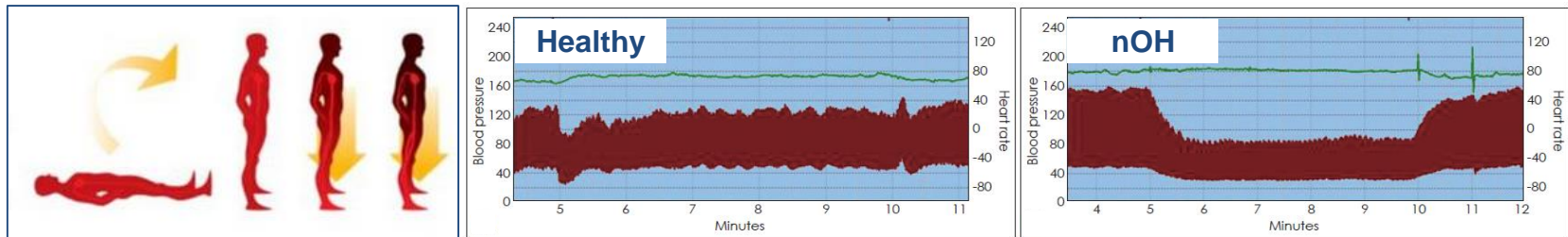
Objectives	Results from First Cohort of Patients at 80 mg	
Evaluate safety	✓	<ul style="list-style-type: none"> <li>No moderate or severe AEs deemed possibly related to study drug</li> <li>No signal of systemic immunosuppression or changes in lipids</li> </ul>
Confirm PK in UC patients	✓	<ul style="list-style-type: none"> <li>Plasma levels consistent with healthy volunteer SAD/MAD data, minimal systemic exposure in patients</li> </ul>
Confirm drug at site of action	✓	<ul style="list-style-type: none"> <li>Relevant drug concentrations in distal colonic tissue</li> </ul>
Evidence of target engagement by biomarkers	✓	<ul style="list-style-type: none"> <li>Reduction on pSTAT1 in colonic tissue</li> <li>Reductions in serum CRP and fecal calprotectin</li> </ul>
Signals of biologic activity at 4 weeks <sup>1</sup>	✓	<ul style="list-style-type: none"> <li>7 of 10 patients on TD-1473 experienced <math>\geq 1</math>-point reduction in Mayo rectal bleeding subscore, compared to 1 of 3 patients on placebo</li> <li>3 of 10 patients on TD-1473 experienced <math>\geq 1</math>-point reduction in Mayo endoscopic subscore, compared to zero patients on placebo               <ul style="list-style-type: none"> <li><b>Mucosal healing achieved in two patients</b></li> </ul> </li> <li>2 of 10 patients on TD-1473 achieved clinical response by total Mayo Score, compared to zero patients on placebo</li> <li>4 of 10 patients receiving TD-1473 achieved clinical response by partial Mayo score, compared to 1 of 3 patients on placebo</li> </ul>

TD-1473 to advance into multi-dose induction and maintenance study in 2018

<sup>1</sup> Gastroenterology Vol. 148, No. 1, pages 37-51. "Converging Goals of Treatment of Inflammatory Bowel Disease From Clinical Trials and Practice." Levesque, et al. [http://www.gastrojournal.org/article/S0016-5085\(14\)00999-8/pdf](http://www.gastrojournal.org/article/S0016-5085(14)00999-8/pdf)  
 Published online August 12, 2014. Total Mayo Clinic Score (MCS) as referenced herein, with endoscopic subscore modified such that mild friability is scored as a 2 rather than a 1 (pages 39-40). Clinical response for partial MCS consistent with clinical response for MCS, except criteria for clinical response by partial MCS include a decrease in partial MCS of at least 2 points versus 3 points in the MCS criteria. Mucosal healing based on modified Mayo endoscopy score. PRO2-e = rectal bleeding, stool frequency and endoscopy components of total MCB (excludes PGA) CRP = C-Reactive Protein; pSTAT1 = phosphorylated signal transducer and activator of transcription1

# Neurogenic Orthostatic Hypotension (nOH) Represents a Significant Unmet Need

nOH is characterized by a **sustained drop in blood pressure** that occurs **upon standing up** and is associated with the **nervous system**, specifically due to the body producing **insufficient levels of norepinephrine**



- Associated with several autonomic disorders, including Multiple System Atrophy (MSA), Parkinson's Disease (PD), and Pure Autonomic Failure (PAF)
- Orphan indication with <200k patients in US
- Symptoms include dizziness, fainting, blurred vision and weakness
- Significant impacts to QoL for both patients and family members
  - Patients limited in routine daily functions and prone to injury from falling
  - In severe cases, patients become bedridden and require caregiver support

# Current Approved Therapies in Neurogenic Orthostatic Hypotension (nOH) Have Limitations

## Current therapies limited in safety, efficacy, and dosing

- Only droxidopa (Northera) and midodrine are FDA-approved for nOH
- Both are synthetic exogenous NE analogues that impact disease by increasing vascular tone
- Significant unmet need remains due to limitations of current therapies:
  - Supine hypertension (high blood pressure while lying down)
  - Require dosing three times a day
  - Patients may become refractory over time or discontinue due to AEs<sup>1</sup>
  - Effectiveness of droxidopa beyond two weeks has not been established<sup>2</sup>

## Opportunity exists for effective, well tolerated nOH therapies

- TD-9855, a dual norepinephrine and serotonin reuptake inhibitor (NSRI), may lead to significant benefits for patients over existing therapy

Successful nOH therapy would target reduction in symptoms and offer meaningful improvements in quality of life for patients

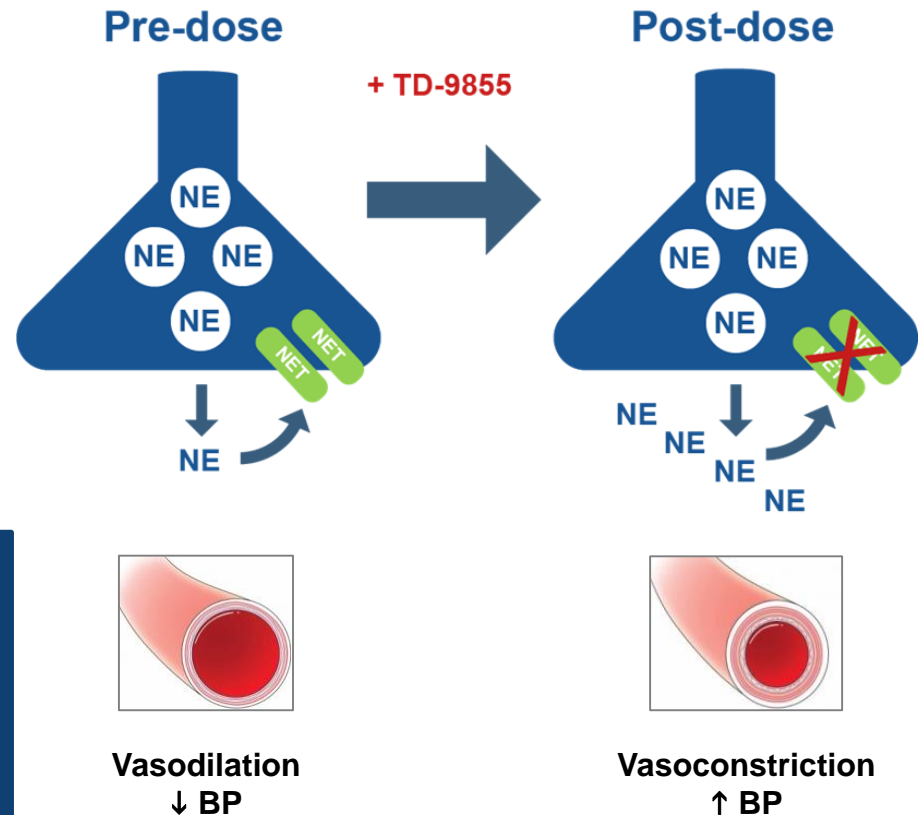
# NET Inhibition with TD-9855 Has Potential to Normalize Vascular Sympathetic Tone in nOH

## A path to treating nOH without introducing exogenous NE

- Blockade of NET in nOH patients inhibits endogenous neuronal NE uptake
- Increased levels of NE in the synapse cause vasoconstriction and a corresponding increase in blood pressure
- Increase in blood pressure improves nOH symptoms

## Rationale for 9855 in nOH

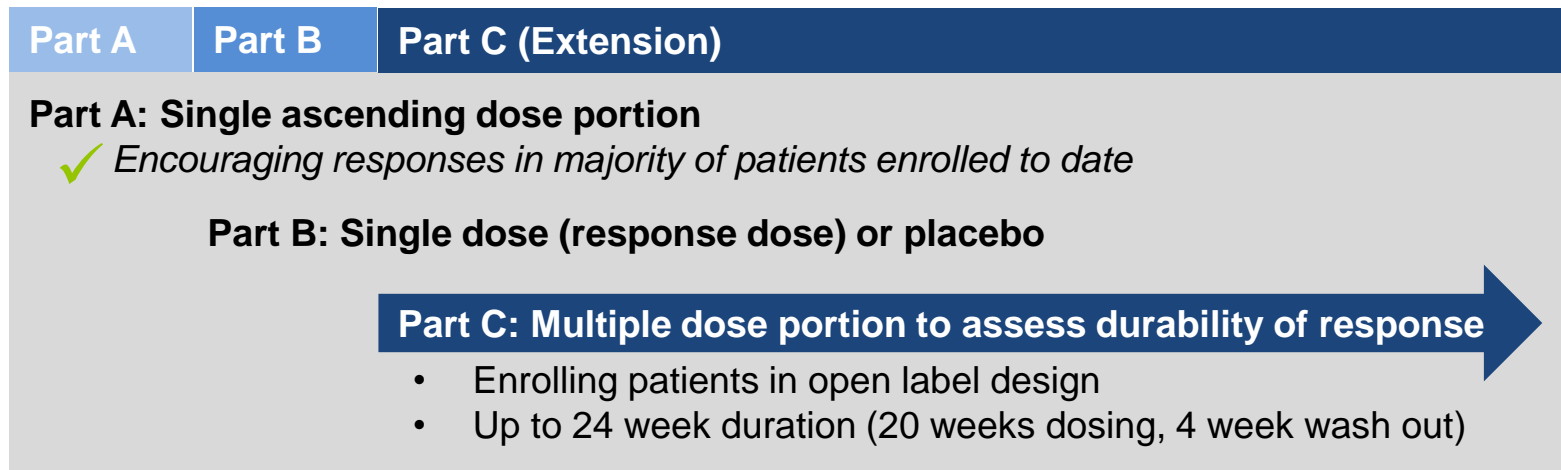
- NE dominance confirmed in humans
- QD dosing, long half-life, and metabolic profile may offer improved patient outcomes
- Favorable safety and tolerability profile established in > 500 subjects<sup>1</sup>



# TD-9855: Phase 2a Study in nOH In Progress, Results Expected 1H 2018

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- **Purpose:** Proof of concept study to evaluate the effect of TD-9855 in improving symptoms of orthostatic intolerance
- **Key endpoints:** Change from placebo in sitting and standing blood pressure, symptom reduction, and safety/tolerability



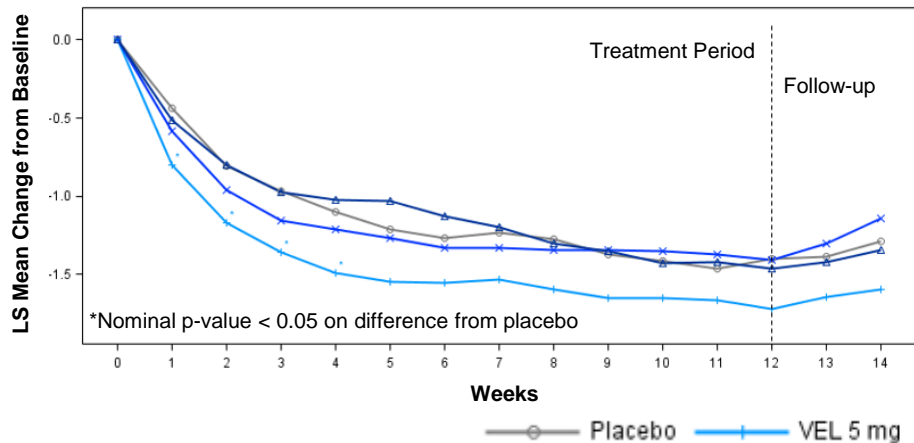
Intention to seek expedited development path



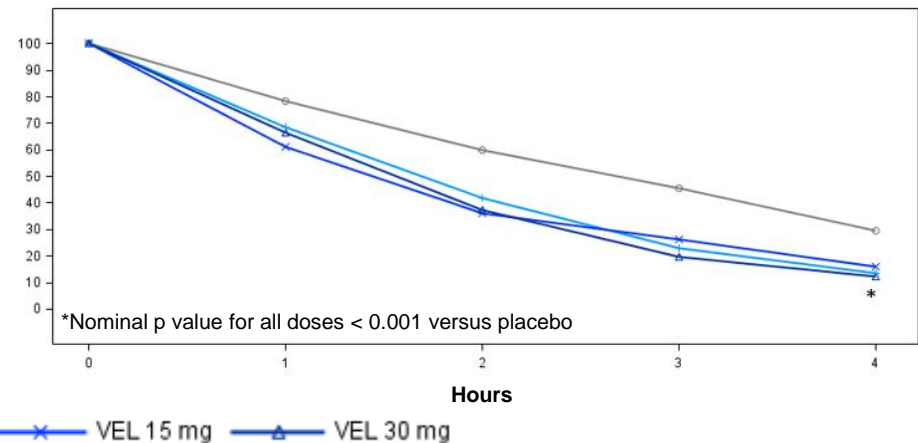
# Velusetrag: Phase 2b Study Provides First Clinical Evaluation of Effect on Gastroparesis Symptoms

- 5 mg demonstrated statistically significant improvements in gastroparesis symptoms compared to placebo
  - 15 and 30 mg doses did not improve symptoms, likely due to side effects at high doses
- All doses significantly improve gastric emptying at 4 hours

### GCSI Total Score



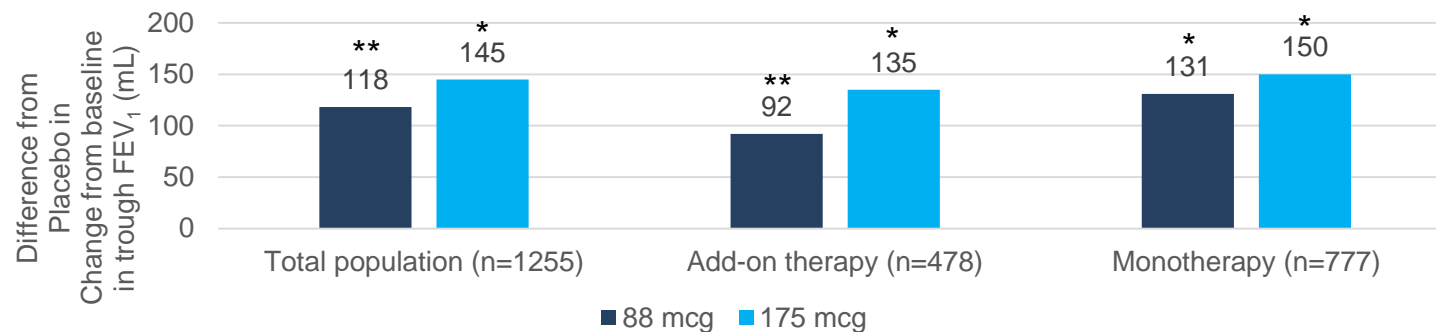
### Scintigraphy Retention % after 28 Days Dosing



Preparing to meet with US and EU regulators to discuss validation of the GRS PRO and next phase of development

# Revefenacin: Phase 3 Registrational Program Complete, with NDA Filing Planned in Late 2017

- Primary endpoint achieved for both doses in both replicate efficacy studies
  - ✓ Robust and sustained improvements in FEV<sub>1</sub>
  - ✓ Effective as monotherapy and as add-on to LABA or LABA/ICS
  - ✓ Generally well tolerated



\* P < 0.0001 versus placebo

\*\* P < 0.001 versus placebo

- Generally well tolerated in 12-month safety study
  - ✓ No new safety issues identified
  - ✓ Rates of adverse events low and comparable to standard of treatment

# Financial Summary

## Select Financial Metrics as of September 30, 2017

	Three Months Ended September 30, 2017 (in thousands)
Product Sales	\$ 4,140
Revenue from Collaborative Arrangements	<u>135</u>
Total Revenue	4,275
Cost of Goods Sold	985
Research and Development <sup>1</sup>	39,343
Selling, General and Administrative <sup>1</sup>	<u>20,944</u>
Total Costs and Expenses	61,272
Operating Loss	\$ (56,997)
<sup>1</sup> Amounts include share-based compensation expense below	
Research and Development	5,005
Selling, General and Administrative	<u>5,680</u>
Total Share-based Compensation Expense	\$ 10,685
Operating Loss excluding Share-based Compensation	\$ (46,312)
Cash, Cash Equivalents and Marketable Securities as of September 30, 2017	\$ 434,400

# GSK's Trelegy Ellipta Offers Significant Potential

## FDA Approval for COPD in September 2017<sup>1</sup>

### Economic interest serves as an important strategic asset

- Upward-tiering royalty 5.5% - 8.5% of worldwide net sales<sup>2</sup>
- Expected to launch in US in mid-November
- Passive economic interest with no cost obligations to TBPH

### Program Summary

- First and only FDA-approved once-daily single inhaler triple therapy comprising an ICS, LAMA and LABA<sup>3</sup>
- FF/UMEC/VI, active components of BREO<sup>®</sup> and ANORO<sup>®4</sup>
- Approved for use in certain COPD patients
- Jointly managed by GSK and Innoviva<sup>5</sup>
- Potential regulatory approval in EU in 2017
- Phase 3 CAPTAIN asthma study underway



### Landmark 10,000-patient IMPACT study in COPD

- ✓ 15% reduction in annual rate of exacerbations compared with Relvar/Breo Ellipta (FF/VI)
- ✓ 25% reduction compared with Anoro Ellipta (UMEC/VI)
- ✓ Significant improvements in lung function at week 52 compared to same dual therapies
- ✓ Improvements also observed in St. George's Respiratory Questionnaire (SGRQ) change from baseline
- ✓ Will support additional regulatory filings planned in 2018

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# About VIBATIV<sup>®</sup> (telavancin)

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VIBATIV was discovered internally in a research program dedicated to finding new antibiotics for serious infections due to *Staphylococcus aureus* and other Gram-positive bacteria, including MRSA. VIBATIV is a bactericidal, once-daily, injectable lipoglycopeptide antibiotic with in vitro potency and a dual mechanism of action whereby telavancin both inhibits bacterial cell wall synthesis and disrupts bacterial cell membrane function.

VIBATIV for injection is approved in the U.S. for the treatment of adult patients for complicated skin & skin structure infections (cSSSI) caused by susceptible isolates of Gram-positive bacteria, including *Staphylococcus aureus*, both methicillin-susceptible (MSSA) and methicillin-resistant (MRSA) strains. In addition, VIBATIV telavancin 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 *Staphylococcus 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 with concurrent bacteremia (in addition to either skin infection or pneumonia).

VIBATIV is indicated in Canada and Russia for complicated skin & skin structure infections and HAP/VAP caused by Gram-positive bacteria, including MRSA.

VIBATIV is indicated in the European Union for the treatment of adults with nosocomial pneumonia (NP) including ventilator associated pneumonia (VAP), known or suspected to be caused by methicillin resistant *Staphylococcus aureus* (MRSA) and should be used only in situations where it is known or suspected that other alternatives are not suitable.

# VIBATIV<sup>®</sup> (telavancin)

## Important Safety Information (US)

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### **Mortality**

Patients with pre-existing moderate/severe renal impairment (CrCl  $\leq$ 50 mL/min) who were treated with VIBATIV<sup>®</sup> 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).