# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, DC 20549**

# FORM 8-K

**Current Report Pursuant**
**to Section 13 or 15(d) of the**
**Securities Exchange Act of 1934**

Date of Report (Date of earliest event Reported): **December 12, 2014**

# THERAVANCE BIOPHARMA, INC.

(Exact Name of Registrant as Specified in its Charter)

| **Cayman Islands** | **001-36033** | **Not Applicable** |
|---|---|---|
| (State or Other Jurisdiction of Incorporation) | (Commission File Number) | (I.R.S. Employer Identification Number) |

**PO Box 309**
**Ugland House, South Church Street**
**George Town, Grand Cayman, Cayman Islands KY1-1104**
**(650) 808-6000**
(Addresses, including zip code, and telephone numbers, including area code, of principal executive offices)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01 Regulation FD Disclosure.**

*The information in this Current Report (including Exhibit 99.1) is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Securities Exchange Act of 1934"), or otherwise subject to the liabilities of that Section. The information in this Current Report (including Exhibit 99.1) shall not be incorporated by reference into any registration statement or other document pursuant to the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.*

Theravance Biopharma, Inc. held an Investor and Analyst Day in New York, NY on Friday, December 12, 2014 from 9:00 to 11:30 EST at which members of management presented updates regarding the post-split business outlook, commercial strategy for VIBATIV® and key development programs. A copy of the slide presentation is furnished as Exhibit 99.1 to this report and is incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit | Description |
|---|---|
| Exhibit 99.1 | Theravance Biopharma's Investor Slide Presentation at Investor and Analyst Day on December 12, 2014 |

**SIGNATURE**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**THERAVANCE BIOPHARMA, INC.**

Date: December 12, 2014

By: /s/ Renee D. Gala
**Renee D. Gala**
**Senior Vice President and Chief Financial Officer**

Theravance Biopharma

Medicines That Make a Difference®

# Introduction to Theravance Biopharma:
# *Strategic Vision and Differentiation*

**Rick E Winningham**

*Chairman and Chief Executive Officer*

# Today's Agenda

| | | |
|---|---|---|
| **Introduction to Theravance Biopharma: Strategic Vision and Differentiation** | **Rick E Winningham**<br>*Chairman and Chief Executive Officer* | **9:00-9:20 a.m.** |
| **VIBATIV® Business Strategy** | **Frank Pasqualone**<br>*SVP, Operations* | **9:20-9:35 a.m.** |
| **Telavancin: A Clinician's Perspective** | **Louis D. Saravolatz, MD, MACP**<br>*St. John Hospital, Detroit, MI*<br>*Infectious Disease Specialist* | **9:35-9:50 a.m.** |
| **Q&A Session #1** | | **9:50-10:00 a.m.** |
| **Break** | | **10:00-10:10 a.m.** |
| **TD-4208: Nebulized LAMA for COPD**<br>**Axelopran: Oral PuMA for OIC** | **Brett Haumann, MD, MBA**<br>*SVP, Clinical Development and Operations* | **10:10-10:40 a.m.** |
| **R&D: Evolution of Insight and Approach** | **Mathai Mammen, MD, PhD**<br>*SVP, Research & Development* | **10:40-10:55 a.m.** |
| **Financial Highlights and Outlook** | **Renee Gala**<br>*SVP and Chief Financial Officer* | **10:55-11:00 a.m.** |
| **Closing Remarks** | **Rick Winningham**<br>*Chairman and Chief Executive Officer* | **11:00-11:05 a.m.** |
| **Q&A Session #2** | | **11:05-11:15 a.m.** |

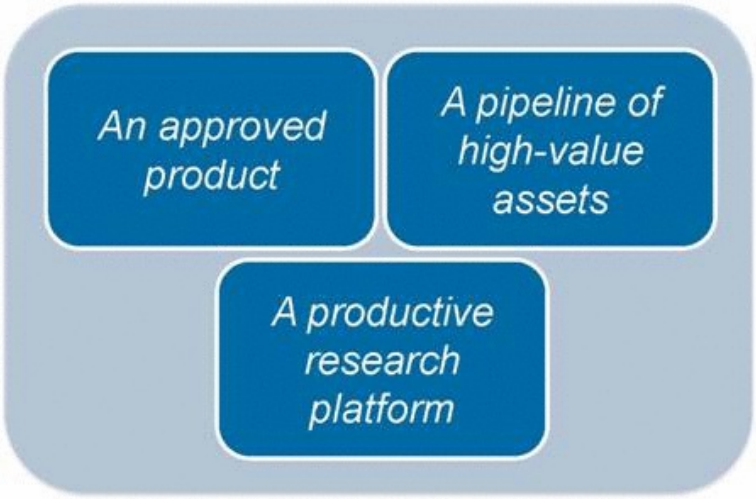
# Safe Harbor Statement

This presentation 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. The words “anticipate”, “expect”, “goal,” “intend”, “objective,” “opportunity,” “plan”, “potential”, “target” and similar expressions are intended to identify such forward-looking statements. Examples of such statements include statements relating to: the strategies, plans and objectives of Theravance Biopharma, the status and timing of clinical studies, data analysis and communication of results, the potential benefits and mechanisms of action of product candidates, the enabling capabilities of Theravance Biopharma's approach to drug discovery and Theravance Biopharma's proprietary insights, expectations for product candidates through development and commercialization (including their potential as components of combination therapies), and the timing of seeking regulatory approval of product candidates. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of this presentation 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: the disruption of operations during the transition period following the spin-off of Theravance Biopharma from Theravance, Inc., including the diversion of management's and employees' attention from the business, adverse impacts upon the progress of discovery and development efforts, disruption of relationships with collaborators and increased employee turnover, 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), 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 products and risks associated with establishing distribution capabilities for telavancin with appropriate technical 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, 2014. 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.

# Theravance Biopharma **Today**

**(NASDAQ: TBPH)**

***Theravance Biopharma was created to drive value from a unique and diverse set of assets***

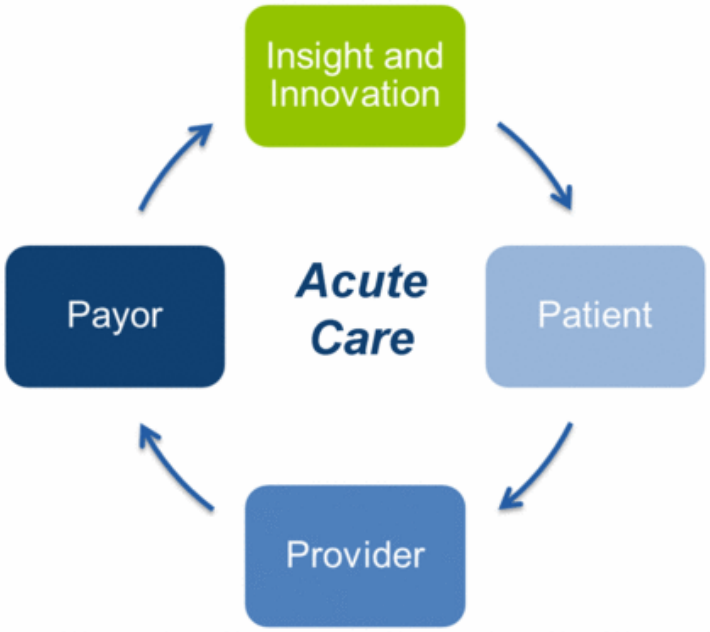


# **Strategic Anchors** for Our Business
# Guiding Principles for How We Operate

- *Focus on **Insight** and **Innovation***
- ***Outsource** Non-core Activities*
- *Create and Foster an **Integrated Environment***
- *Aggressively **Manage Uncertainty***

# The Theravance Biopharma **Strategy**

***Leverage Our Insights to Make a Difference for Patients and Create Meaningful Value for Shareholders***



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# The Theravance Biopharma **Strategy**

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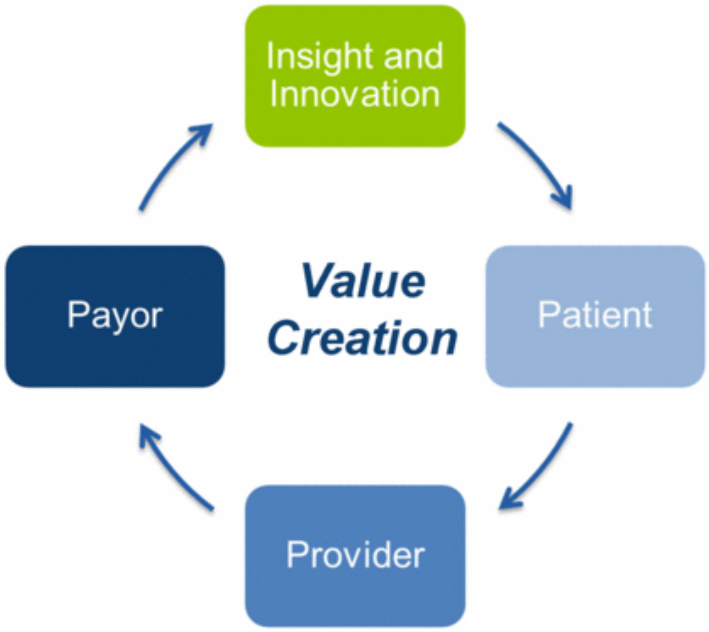




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# Commercializing **Our Products**

## Translating Insight and Innovation into Value Creation




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# Enhanced Opportunities for **Value Creation**

## **Focus on Infectious Disease, Lung** and **GI**

| | Late-stage | Mid-stage |
|---|---|---|
| Infectious Disease / Other | VIBATIV:<br>cSSSI<br>HABP/VABP<br>(Bacteremia) | TD-6450 (HCV)<br>TD-1792, TD-1607 (MRSA)<br>TD-9855 (Fatigue) |
| Lung | TD-4208 (COPD)<br>Closed Triple (COPD) | MABA (COPD)<br>MABA-ICS (COPD, Asthma) |
| GI Tract | Axelopran (OIC)<br>Axelopran/Opioid FDC | Velusetrag (GP)<br>TD-8954 (ICU IV prokinetic) |

*Notes: Late-stage includes approved products, assets in Phase 3 development, and Phase 3-ready; Mid-stage includes assets between Phase 1 and Phase 2b.*

# Enhanced Opportunities for **Value Creation**

## **Strategic Partnerships** / **Partner Funded** Programs

| | Late-stage | Mid-stage |
|---|---|---|
| Infectious Disease / Other | VIBATIV:<br>cSSSI<br>HABP/VABP<br>(Bacteremia) | TD-6450 (HCV)<br>TD-1792, TD-1607 (MRSA)<br>TD-9855 (Fatigue) |
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*Notes: Late-stage includes approved products, assets in Phase 3 development, and Phase 3-ready; Mid-stage includes assets between Phase 1 and Phase 2b.*



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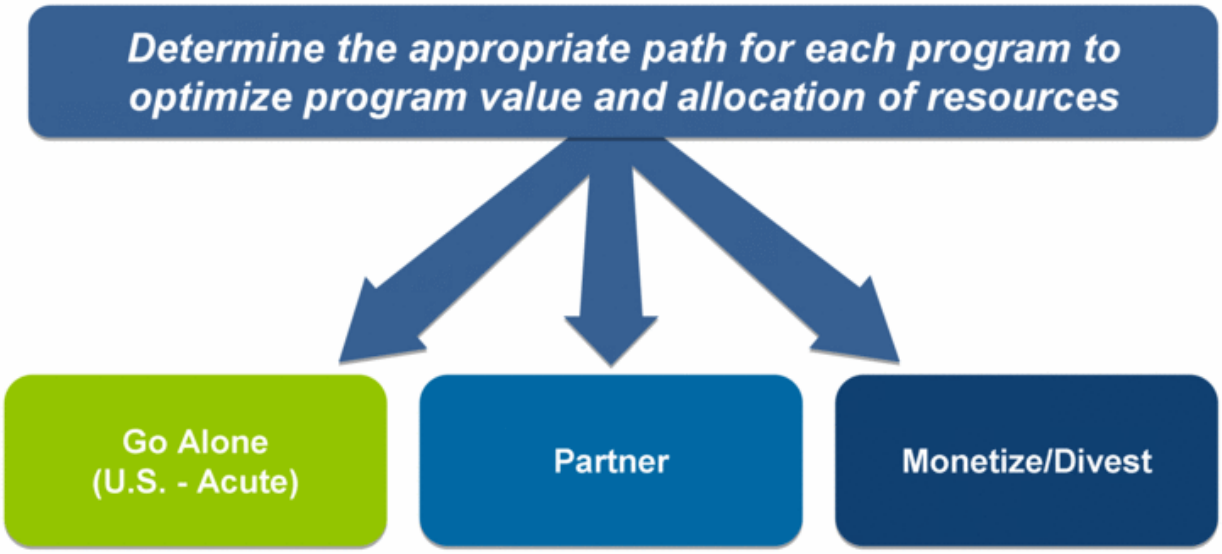
# Manage Our Portfolio

## Pipeline Provides Strategic Options



# Commercializing **Our Products**

## Focus on **VIBATIV®**

| | |
|---|---|
| **Therapeutic Focus:** | ↗ Serious MRSA infections (approved for cSSSI and HABP/VABP, Phase 3 for bacteremia) |
| **Product Attributes:** | ↗ Treatment for Gram-positive serious infection across multiple body sites<br>↗ Dual mechanism of action |
| **Partnering Strategy:** | ↗ Regional partners contribute cash plus insight to drive commercial success |
| **Go To Market Approach:** | ↗ Build commercial infrastructure with acute care focus and highly experienced institutional reps<br>↗ Significant medical information component |

**Go Alone (U.S. - Acute)** | **Partner** | **Monetize/Divest**

# Leveraging Our Commercial Infrastructure

## Patients Who Cycle Through Acute Care Settings

- Developing products initiated or used in and around acute care centers leverages existing commercial infrastructure

**Acute Care Center Opportunities**

| MRSA | COPD | Pain | ICU Nutrition |
|---|---|---|---|
| VIBATIV | TD-4208 | Axelopran | TD-8954 |
| TD-1792 | | Axelopran/ | |
| TD-1607 | **Gastroparesis** | Opioid FDC | **Heart Failure** |
| | Velusetrag | | ARNI |

- Strategic commercial partnerships to expand reach will be key in certain specialty markets and outside the U.S.

# Commercializing **Our Products**

## Focus on **TD-4208**

| | |
|---|---|
| **Therapeutic Focus:** | ↗ Respiratory: COPD and other diseases of lung |
| **Product Attributes:** | ↗ Potential first-in-class nebulized, once-daily bronchodilator designed to selectively target the lung without significant exposure |
| | ↗ Compatible with requirements for DPI/MDI presentation requirements |
| **Partnering Strategy:** | ↗ Partner for commercialization in certain segments |
| | ↗ Partner for DPI/MDI and/or combination therapies |
| **Go To Market Approach:** | ↗ Rely on our U.S. commercial infrastructure for nebulized therapy initiated and/or prescribed in acute care setting |
| | ↗ Leverage partner in other market segments |

**Go Alone (U.S. - Acute)** | **Partner** | **Monetize/Divest**

# Commercializing **Our Products**

## Focus on **Axelopran** and **Opioid/Axelopran Fixed Dose Combo**

| | |
|---|---|
| **Therapeutic Focus:** | ↗ GI: Opioid-induced constipation (OIC)<br>↗ Pain: Fixed-Dose Combo (FDC) with opioid |
| **Product Attributes:** | ↗ Potential best-in-class, orally-administered and peripherally selective opioid receptor antagonist for treatment of OIC, designed for high target selectivity and no impact on opioid analgesia<br>↗ May be co-formulated with opioid |
| **Partnering Strategy:** | ↗ Leverage partner for funding / commercialization |
| **Go To Market Approach:** | ↗ Rely on our infrastructure for OIC or FDC therapy initiated and/or prescribed in acute care setting<br>↗ Leverage partner in other market segments |

Go Alone (U.S. - Acute) | **Partner** | Monetize/Divest

# Commercializing **Our Products**

## Focus on **Velusetrag**

| | |
|---|---|
| **Therapeutic Focus:** | ↗ GI: Gastroparesis |
| **Product Attributes:** | ↗ Oral, once-daily highly selective 5-HT4 agonist<br>↗ Accelerated gastric emptying in Phase 2a study |
| **Partnering Strategy:** | ↗ Partnered with Alfa Wassermann (AW) for EU, Russia, China and Mexico<br>↗ Rights retained in U.S., Canada and Japan<br>↗ AW to fund ~90% of Phase 2b gastroparesis study initiating late 2014/early 2015 |
| **Go To Market Approach:** | ↗ Hospital-focused commercial team well positioned to influence at critical juncture<br>↗ Leverage partner for commercialization outside U.S. |

**Go Alone (U.S. - Acute)** | **Partner** | **Monetize/Divest**

# Leveraging **Monetization/Divestment**

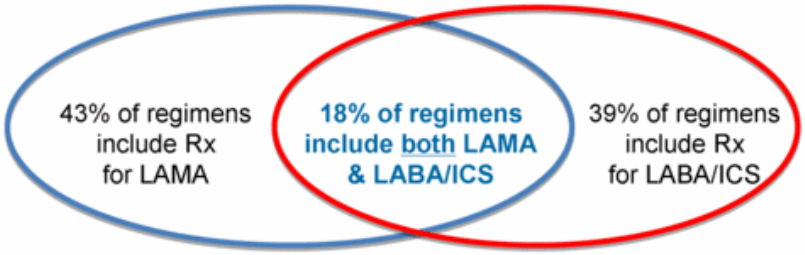
## Focus on **Closed Triple**

| | |
|---|---|
| **Therapeutic Focus:** | ↗ Respiratory: COPD and potentially asthma |
| **Product Attributes:** | ↗ Potential first-in-class once-daily closed triple therapy in LABA/LAMA/ICS<br>↗ Triple therapy targeted towards patients with more symptoms and higher exacerbation risk |
| **Partnering Strategy:** | ↗ TBPH retains economic interest<br>↗ Development and commercialization funded 100% by GSK |
| **Go To Market Approach:** | ↗ Full reliance on GSK for development and commercialization<br>↗ Jointly managed by GSK and Theravance, Inc. (Royalty Management Co.) |

Go Alone (U.S. - Acute) | Partner | **Monetize/Divest**

# GSK/Theravance Closed Triple Addresses a **Significant**, **Growing** and **High Value Patient Segment**

- 18% of prescribed COPD regimens include co-Rx for LAMA+LABA/ICS[1]




- Patients on triple therapy **constitute highest value/greatest need segment**
  - These patients represent >40% of total LAMA and ICS/LABA COPD sales (**estimated $2.1B out of $4.6 total annual US sales** of LAMA and LABA/ICS products for COPD)[1,2]
  - Triple patients have more symptoms + higher exacerbation risk. Greater disease burden for patient and healthcare system = greater value for treatment success
- GSK/Theravance have the **only QD closed triple in late stage** development
  - Phase 3 ongoing in 12K patients; Two positive Phase 3 studies completed in "open" triple therapy



[1]Encuity Research, LLC., *TreatmentAnswers*™ (2013)
[2]EvaluatePharma (2013)

# The Theravance Biopharma **Difference**

- Focused acute care, commercial strategy on internally discovered product **VIBATIV**
  - **Pipeline** of internally discovered product candidates
  - Productive research organization to drive innovation value
- Team **track record** of approvals: 5 indications in 3 drugs in 13 years
- Economic interest in certain GSK programs†, including "**Closed Triple**"
- Efficient corporate structure, with tax domicile outside the U.S.
- Strong balance sheet with **$350M cash**‡ (as of 9/30/2014)
  - Invest $150-160M in the business in 2015

*† TBPH holds economic interest in future payments that may be made by GlaxoSmithKline plc (GSK) relating to certain programs, including "Closed Triple" (FF/UMEC/VI) (Fluticasone Furoate/Umeclidinium/Vilanterol), MABA/FF ('081), MABA monotherapy and other future products that may be combined with VI or MABA '081.*
*‡ Includes cash, cash equivalents and marketable securities.*



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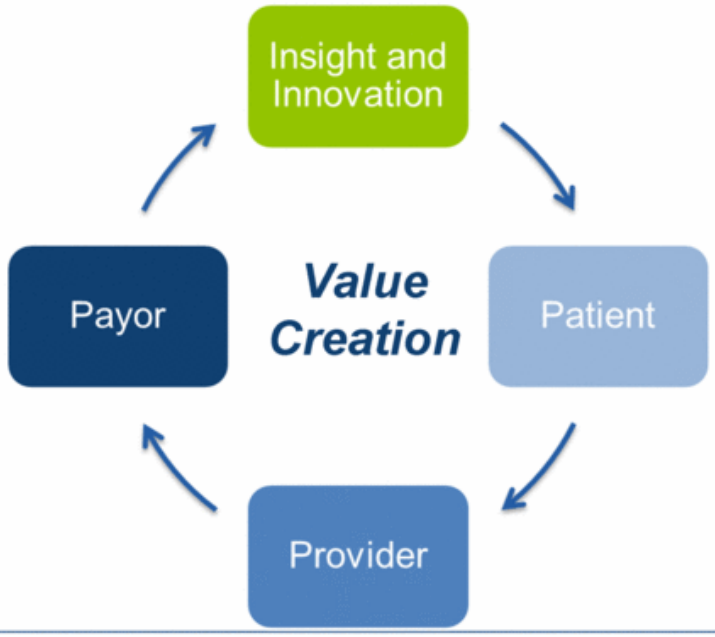
# The Theravance Biopharma **Strategy**

***Leverage Our Insights to Make a Difference for Patients and Create Meaningful Value for Shareholders***



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Medicines That Make a Difference®

# VIBATIV®
## *Business Strategy*

**Frank Pasqualone**

*Senior Vice President of Operations*

# What is **VIBATIV®** (telavancin)?

**The first FDA approved lipoglycopeptide exhibiting concentration-dependent bactericidal activity via a dual mechanism of action that inhibits cell wall synthesis and disrupts membrane barrier function**

**Active against Gram-positive bacteria, including** methicillin-resistant *Staphylococcus aureus* (**MRSA**)

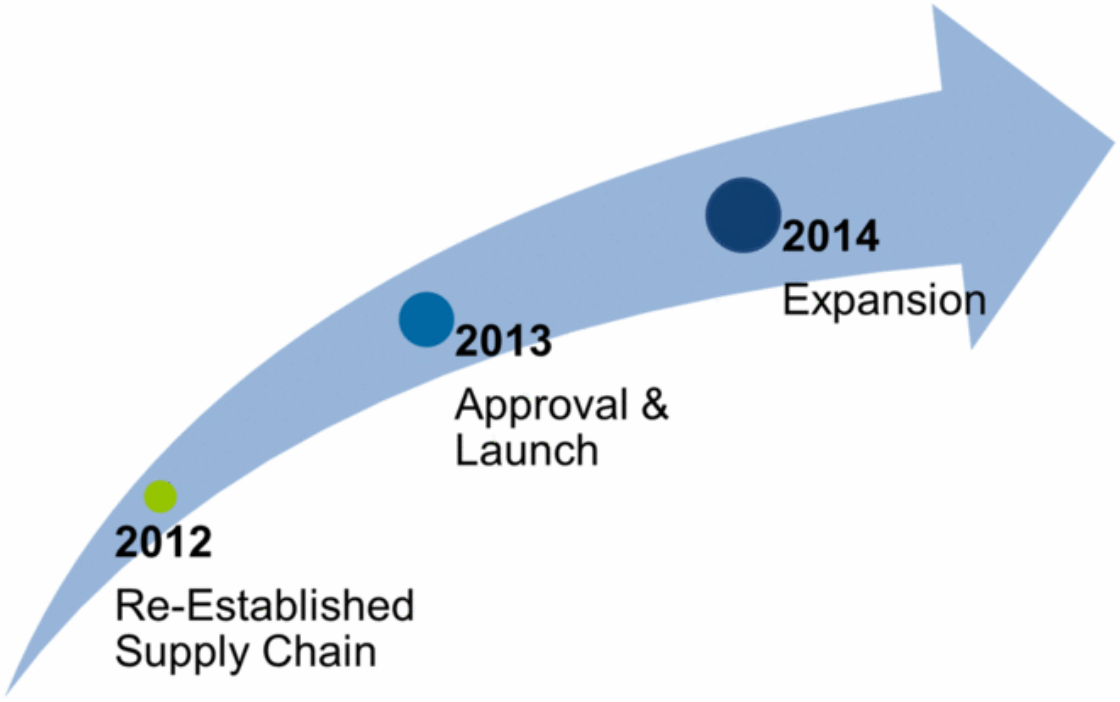
Intravenously administered; **once-daily dosing**

Approved in the U.S. for treatment of the following infections in **adult patients** caused by designated susceptible bacteria:

- Complicated skin and skin structure infections (cSSSI)
- Hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) caused by susceptible isolates of *Staphylococcus aureus* when alternative treatments are not suitable

# Transforming **VIBATIV**

## Efficient Transition to Acute Care



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# VIBATIV

## Potential for Broadest Set of Indications[1]

| Compound | Indications SSSI* | HABP/VABP | Bacteremia |
|---|---|---|---|
| **telavancin** | ✓ | ✓ | **Registrational Study** |
| ceftaroline | ✓ | | |
| dalbavancin | ✓ | | |
| daptomycin | ✓ | | ✓ |
| linezolid | ✓ | ✓ | |
| oritavancin | ✓ | | |
| tedizolid | ✓ | | |



(*) Complicated or Acute Bacterial Skin or Skin Structure Infection

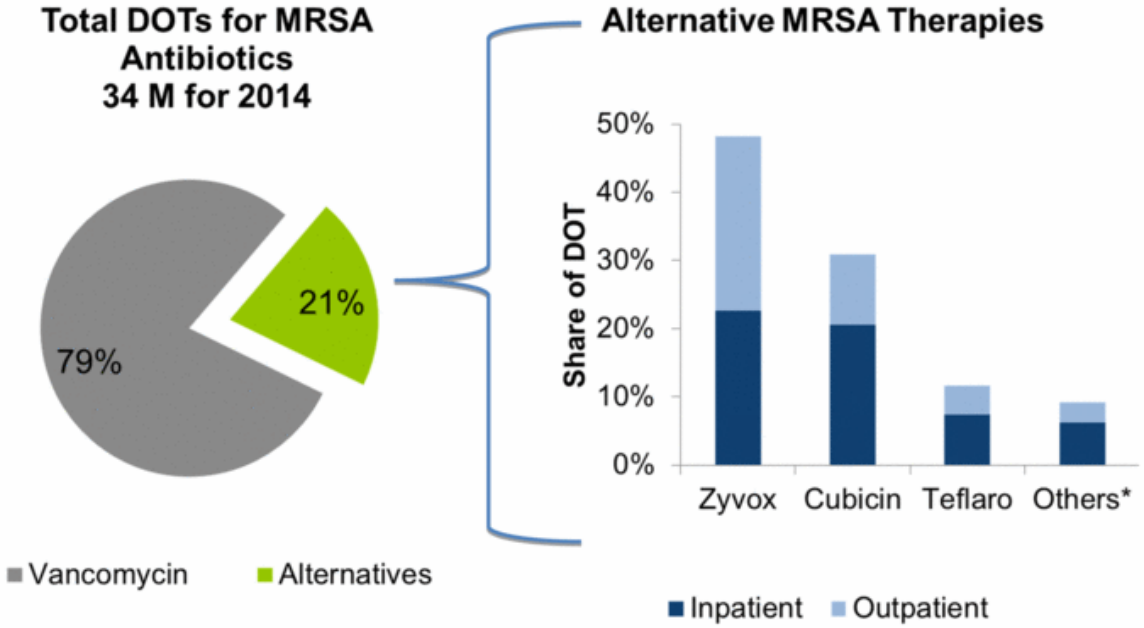
[1]Potential for broadest set of indications among branded anti MRSA agents

# Theravance Biopharma Difference: Strategy

## Science Delivering Value

| Astellas | | Theravance Biopharma |
|---|---|---|
| 1st line use in the competitive cSSSI population | **Position** | VIBATIV is the preferred anti-MRSA treatment for patients not likely to respond to current *S. aureus* therapy in approved indications |
| None | **Development** | SA Bacteremia, Registry, Pediatric |
| Limited to cSSSI strategy | **Promotion** | Targeted geographic, channel and prescriber strategy for both cSSSI and HABP/VABP |
| Discounted | **Price** | Value-Based Price |

# Current U.S. Market Opportunities Exist for **VIBATIV** Among Alternative MRSA Therapies






Source: TBPH estimates based on integrating data from multiple sources
*Others includes Tygacil and Synercid

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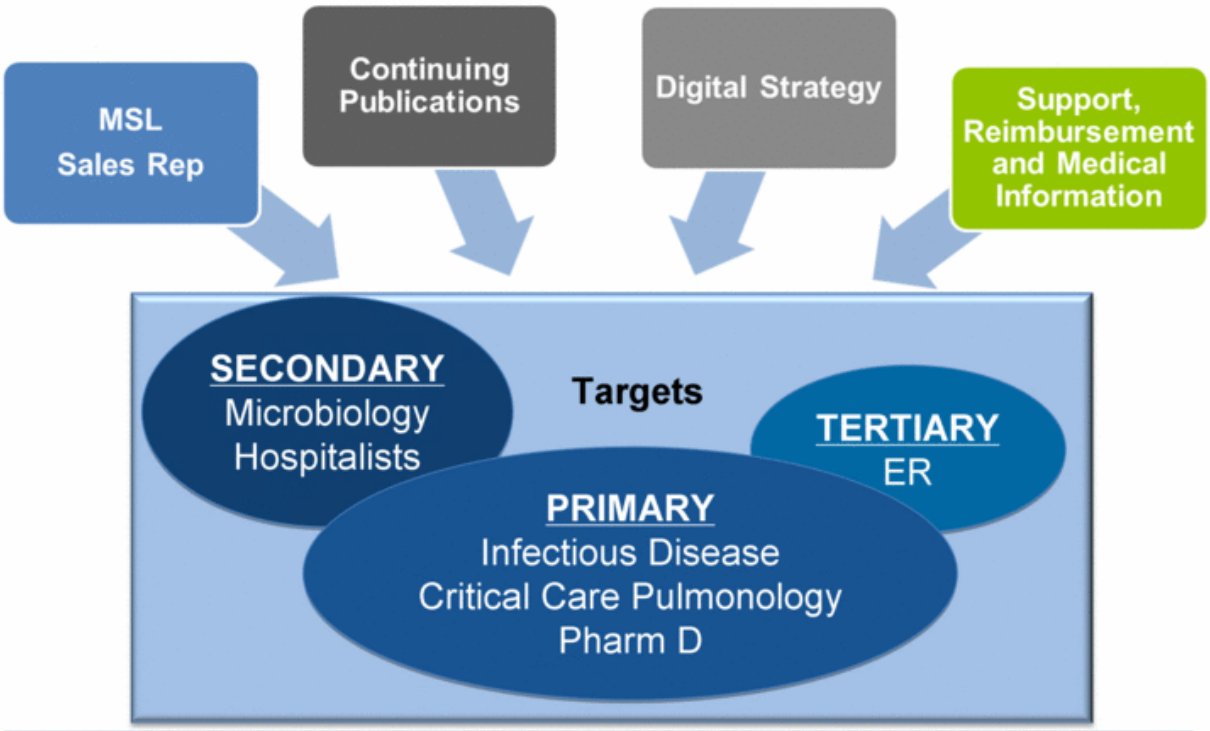
# VIBATIV Approach

## Deliberate and Targeted



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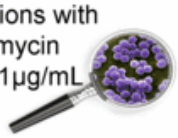
# The Approach Targets Appropriate Patient Populations

HABP/VABP in institutions with vancomycin MICs≥1µg/mL



HABP/VABP patients with comorbidities

Immunocompromised patients

When a bactericidal agent with good tissue penetration is needed

Patients with persistent or recurrent infection

Requiring >7 days of therapy

OPAT*– given convenience of QD dosing

Taking SSRI's

(*) OPAT is defined as Outpatient Parenteral Antimicrobial Therapy

# Market Research

## Supports the Deliberate and Targeted Approach

Former users welcome **VIBATIV** back into the market - good **past performance**; and physicians understand why it left the market

Key differentiating **benefits** of **VIBATIV** are said to be its activity when vancomycin MICs rise, once daily dosing convenience, and bactericidal action

**Key Messages**

Physicians using **VIBATIV** for patients with **an inadequate response** (or contraindication) to vancomycin

Data for **bacteremia** or osteomyelitis would be welcome since there is an unmet need in those indications

VIBATIV® (telavancin)Test Market Initiative: Wave 2, Qualitative Research with Test Market Physicians, Naxion Research: Final Report; September 30, 2014

# The Future

## Building the **VIBATIV** Brand

### Phase III Registrational Bacteremia Trial

- Multicenter, randomized, open-label, non-inferiority trial in 250 patients
- For complicated *Staphylococcus aureus* (SA) bacteremia and SA right-sided infective endocarditis (RIE)

### Publications

- Generate medical/scientific publications to address information gaps
- Over 500 publications* to date

### tour

telavancin observational use registry

- Characterize real-world use of telavancin in 1,000 patients
- Generate data on VIBATIV clinical effectiveness and safety

### Investigator Initiated Research

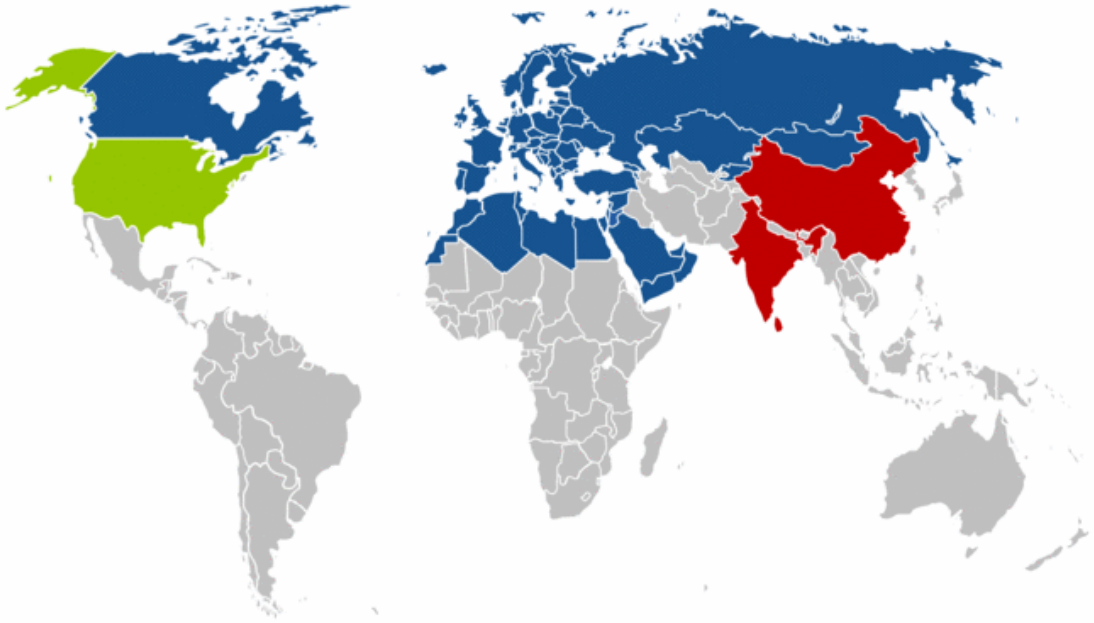
- Focused on evaluating *in vitro* potential/additional indications, appropriate use, and special populations
- 18 active IIR studies in 2014

(*) Publications include: abstracts, manuscripts, posters, and presentations

# The Future

## Building the Global **VIBATIV** Brand

Theravance Biopharma | Partner Presence | Ongoing Partner Discussions





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# Theravance Biopharma Difference

## Foundation Built on **VIBATIV**

- **VIBATIV**:
  - Attractive commercial brand
  - Potential for broadest set of indications[1]
  - Strong IP position
- Market feedback validates brand and commercial strategy
- Foundation for an acute care business within TBPH with the potential for significant value generation




(*) Complicated or Acute Bacterial Skin or Skin Structure Infection
[1]Potential for broadest set of indications among branded anti MRSA agents

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# Telavancin: A Clinician's Perspective

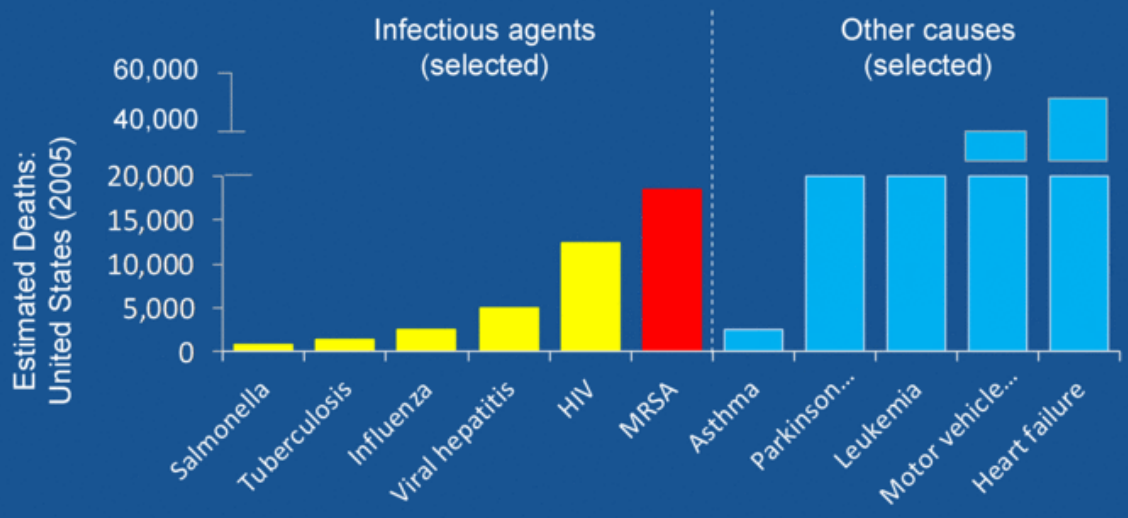
Louis D. Saravolatz, MD, MACP
St. John Hospital, Detroit, MI
Infectious Disease Specialist

Disclosure: Theravance Biopharma Antibiotics Scientific Advisor

# The Challenge of MRSA in the United States

## U.S. Mortality Rates in Infectious Diseases and Other Causes

- MRSA is responsible for more US deaths annually than many other serious infectious diseases




DeLeo, *J Clin Invest.* 2009;119:2464-2474

# The Challenge of MRSA in the U.S.

## MRSA is an ongoing challenge in the community and hospitals

- Over 50% of infections caused by *Staphylococcus aureus* are methicillin-resistant *S. aureus* (MRSA)
- MRSA is among the most common hospital-acquired pathogens
- Serious MRSA infections require prompt and effective treatment
- Clinicians must navigate ongoing concerns over:
  - Clinical efficacy and appropriate dosing with vancomycin
  - Emergence of resistance to standard anti-MRSA therapies

Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. Sievert, et.al.
*Infection Control and Hospital Epidemiology*, Vol. 34, No. 1 (January 2013), pp. 1-14

# The Challenge of Serious Infections: Bacterial Pneumonia

## Hospital-acquired and Ventilator-associated Bacterial Pneumonia (HABP/VABP)

- Second most common hospital-acquired infection in the US
- Up to 27% of all ICU infections are caused by HABP/VABP
  - Results in over 50% of antibiotics prescribed in the ICU
- VABP is estimated to occur in 9% to 27% of all intubated patients
- HABP/VABP is associated with the highest rate of mortality among all hospital-acquired infections
  - HABP/VABP all-cause mortality ranges from 20 - 50%
- HABP/VABP increases patient length of hospital stay and cost of care

Richards, Crit Care Med, 1999, 27(5):887-92; ATS/IDSA 2005, Am J of Resp Crit Care Med; 171, 388-416; CDC Resp Care. 1994;39:1191-1192; Bekaert, *AJRCCM*. 2011;184:1133-39; Fagon, *Am J Med*. 1993;94:281-288; Craven, *Am Rev Resp Dis*. 1986;133:792-796; Flanders, *Am J Inf Ctrl*, 2006;34(2):84-93; Nguile-Makao, *ICM*, 2010;36:781-789.

# The Challenge of Treating HABP/VABP

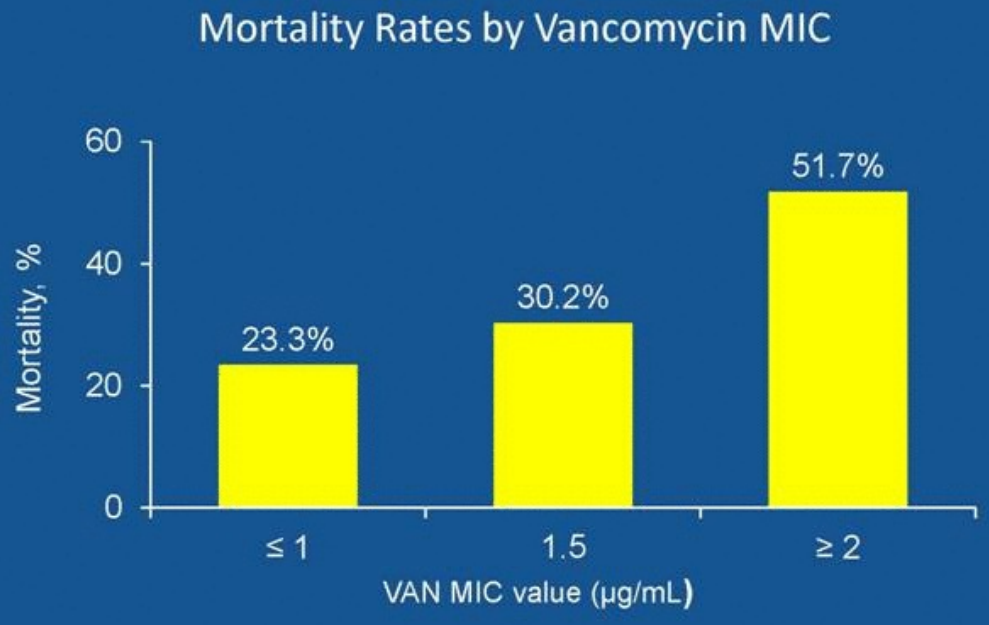
## Significant impact on morbidity, mortality and cost of care

- MRSA is the most common Gram-positive pathogen in HABP/VABP
- Early and appropriate therapy is critical
  - In ICU patients, research demonstrated that early, appropriate antimicrobial therapy is associated with:
    - Shorter duration of antibiotic therapy
    - Decreased length of ICU or hospital stay
    - Decreased mortality
      - Appropriate therapy reduces infection-related and all-cause mortality
    - Lower total cost of care
- Each patient requires individual assessment and decisions on care

Rong, et al. *Ann Pharmacother.* 2010,44:844-850; Hawser, et al. *IJAA.* 2011, 37:219-24; Choi, et al. *ICM.* 2011, 37:63; Moise, et al. *JAC.* 2008, 61:85–90; Lodise, et al. *JAC.* 2008, 62:1138-41; Van Hal, et al. *CID.* 2012,54:755-71

# The Challenge of HABP/VABP due to MRSA Infection

## Higher Vancomycin MICs are Associated with Increased Mortality




Haque et al, Chest, 2010, 138:1356-62

# Individualization of Care

## Treatment Decisions must be made at the Individual Patient Level

- Determine severity of infection
- Cover likely pathogens with empiric therapy
  - Patient history
  - Local epidemiology
- Assess comorbid conditions, including renal function
- Choose appropriate therapy and dose for the patient
- Monitor for efficacy and safety
  - Reassess after obtaining microbiology results

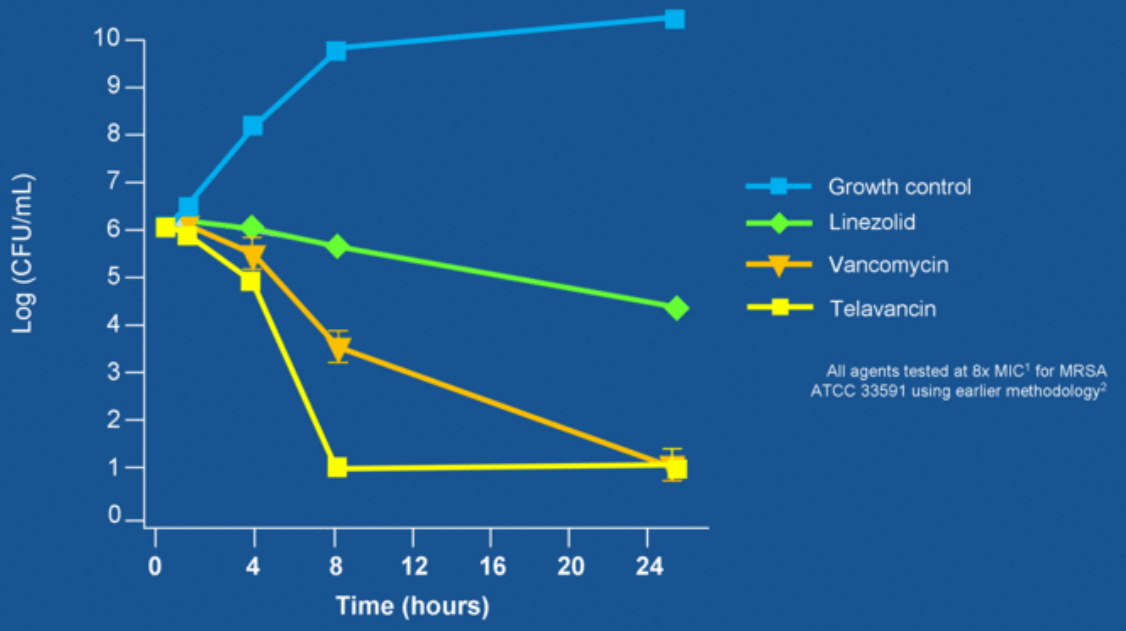
# Why Physicians Choose Telavancin

| Potent Activity |
| --- |
| Dual Mechanism of Action; Bactericidal against clinically important Gram+ organisms |
| Active against *S. aureus* strains with reduced susceptibility to other agents<br>• VAN MIC ≥ 1 µg/mL<br>• VISA, hVISA strains<br>• Daptomycin and linezolid-resistant |
| No resistance identified in clinical trials or in ongoing global surveillance to date |

| Clinically Relevant |
| --- |
| Penetration into important sites of infection, including the lung |
| Drug levels remain above the $MIC_{90}$ for MRSA over 24 hours |
| Clinical efficacy shown in largest HABP/VABP studies to date in a broad population of patients with multiple co-morbidities |
| Convenience of once daily dosing (with no therapeutic dose monitoring) |
| Safety profile characterized in large clinical studies in both cSSSI and HABP/VABP |

# Bactericidal Activity against MRSA

## *In Vitro* Time-Kill Curves




All agents tested at 8x MIC[1] for MRSA ATCC 33591 using earlier methodology[2]

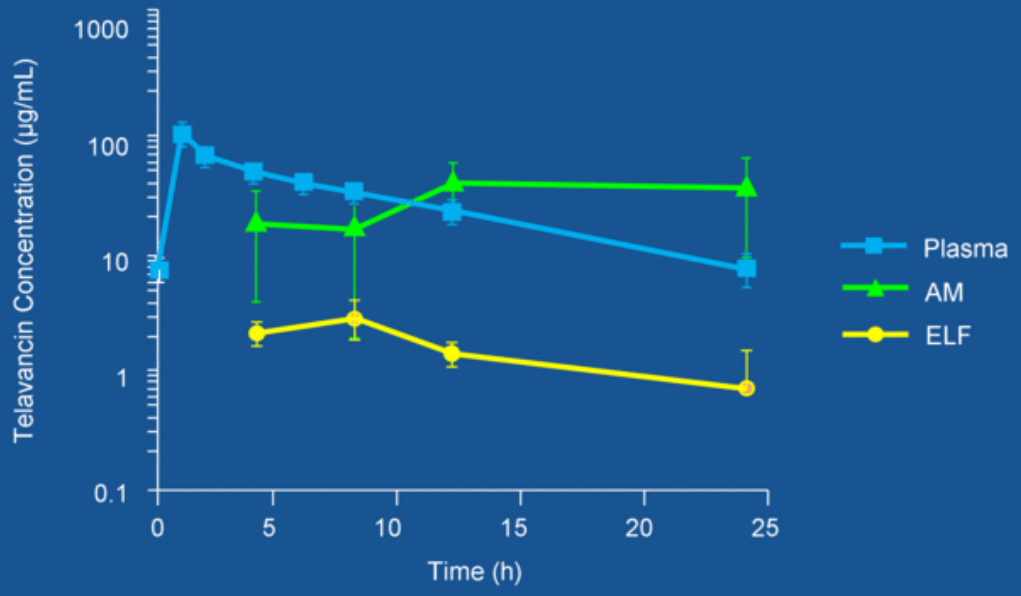
Pace, AAC, 2003;47(11):3602-3604; CLSI. M7 A9

41

# Telavancin lung penetration for treatment of HABP/VABP

## Concentration in Plasma, Alveolar (AM) and Epithelial Lining Fluid (ELF)

Mean (±SD) concentrations of telavancin in plasma, AM, and ELF




Gotfried MH et al. *Antimicrob Agents Chemother.* 2008;52(1):92-97.

# Telavancin Cure Rates in HABP/VABP Phase 3 Clinical Trials

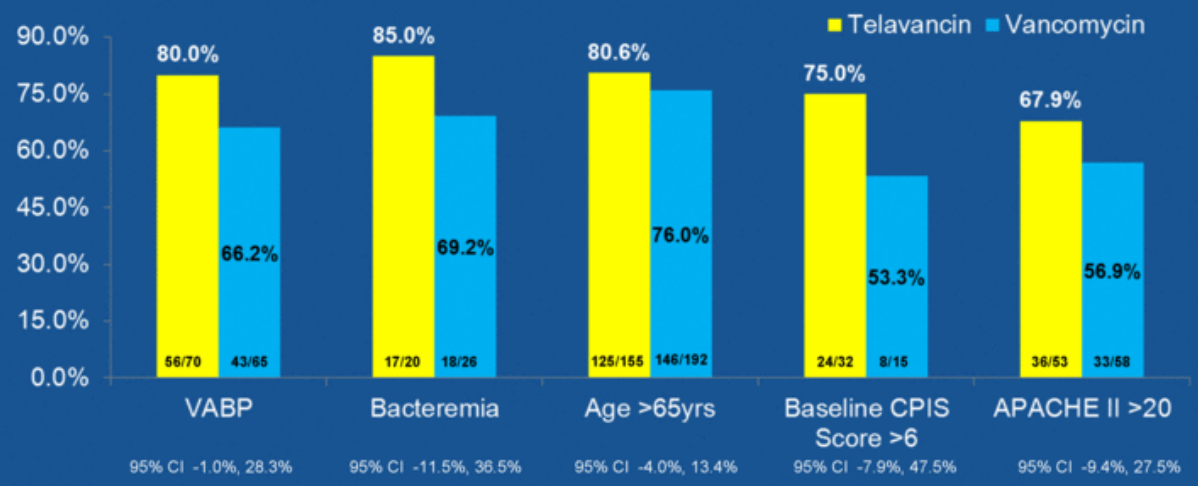
| Study Population | ATTAIN 1 | | ATTAIN 2 | | COMBINED | |
|---|---|---|---|---|---|---|
| | **TLV** | **VAN** | **TLV** | **VAN** | **TLV** | **VAN** |
| **All-Treated (AT)** | 57.5% (214/372) | 59.1% (221/374) | 60.2% (227/377) | 60.0% (228/380) | **58.9%** (441/749) | **59.5%** (449/754) |
| **Difference (95% CI)** | -1.6% (-8.6%, 5.5%) | | 0.2% (-6.8%, 7.2%) | | -0.7% (-5.6%, 4.3%) | |
| **Clinically Evaluable (CE)** | 83.7% (118/141) | 80.2% (138/172) | 81.3% (139/171) | 81.2% (138/170) | **82.4%** (257/312) | **80.7%** (276/342) |
| **Difference (95% CI)** | 3.5% (-5.1%, 12.0%) | | 0.1% (-8.2%, 8.4%) | | 1.7% (-4.3%, 7.7%) | |

| Microbiologically Evaluable (ME) | TLV % Cure | VAN % Cure | % Difference (TLV – VAN; 95% CI) |
|---|---|---|---|
| **Single Gram-positive (only)** | **84.0** (147/175) | **75.9** (132/174) | **8.1 (-0.2%, 16.5%)** |
| **MRSA (only)** | **80.2** (73/91) | **74.1** (86/116) | **6.1 (-5.3%, 17.5%)** |
| ***S. aureus* with VAN MIC ≥ 1 µg/mL** | **85.7** (78/91) | **74.5** (79/106) | **11.2 (0.2%, 22.2%)** |

VIBATIV® (telavancin) Prescribing Information. Theravance Biopharma Antibiotics, Inc. March 2014
Data on File. Theravance Biopharma, Inc.

# Efficacy in Clinically Relevant HABP/VABP Patient Subgroups

## Pooled Clinical Cure Rates by Subgroup in Phase 3 Trials (CE population)




Rubinstein, Crit Care Conf: 29th Internatl. Symposium on Intensive Care and Emergency Med. 13 (pp S128), 2009; Shorr. ATS 2013 (poster); Stryjewski. Int J Antimicro Agents. 2013 Jul 25. pii: S0924-8579(13).

# HABP Patient Successfully Treated with Telavancin

- 57 yo. male smoker readmitted to hospital due to post-operative complications from surgical intervention for wound infection.
  - Prior hospital admission was within prior 3 months (1 week in ICU post-op) and prior antibiotic treatment.
  - Medical history includes COPD, CHF, LVH, CAD, C. diff Colitis and chronic pain due to non-healing wound.
  - T = 99, RR = 26, BP = 134 / 89
  - CrCL = 61 mL/min, WBC = 2,800, Platelets = 45,000
- Develops purulent sputum, rales and slight dyspnea
  - Chest X-ray abnormal with pleural effusion on the left
  - Sputum Gram stain: numerous PMN's, Gram(+) cocci
  - Diagnosed as aspiration pneumonia (HABP)
- MRSA isolated (VAN MIC = 0.5); Prior exposure to VAN and daptomycin
- Switched from vancomycin (1 day, 2 doses) to TLV 10mg/kg for 9.5 days
  - Full resolution of clinical signs/symptoms of HABP
  - No sputum production/sample by day 4 - presumptive microbiologic cure.

# HABP Patient Successfully Treated with Telavancin

- 49 yo. male admitted for Shortness of Breath (SOB), dyspnea and fever
  - Medical history includes: urinary retention and renal abscess. Previously treated for MRSA bacteremia and UTI with vancomycin and daptomycin.
  - T = 101.6; CrCL = 75mL/min, WBC = 13.6
  - Started on vancomycin 1g IV Q12
  - Bacteremia diagnosed (likely due to renal abscess)
  - MRSA isolated (VAN MIC 1.0; daptomycin MIC 0.25; linezolid MIC 2.0)
- Day 4: Remained febrile/spiking 101, Clinically unimproved, elevated WBC
  - Purulent sputum positive for MRSA (vancomycin MIC 1.0)
  - Chest X-ray taken - indicated lower left lobe (LLL) pneumonia with some right lower lobe consolidation: possible bilateral pneumonia
- Day 5: ID consult - patient switched to telavancin 10mg/kg (600mg) daily
  - Afebrile in 48-72 hrs; WBC 6800 in 4 days, blood culture negative 2 of 2 and clinically improved (no SOB, no sputum to culture - presumed MRSA eradication)
  - Patient discharged 19 days post-admission on telavancin outpatient therapy (6wks)
- Re-admission several months later for surgical procedure - confirmed no renal issues (per Scr and CrCl post-treatment) as well as clinical and microbiologic cure

# Effective Treatment for Serious Infections, including HABP/VABP due to MRSA, is Critical

- For the public health
  - Increasing incidence and severity of MRSA infections
  - Increasing burden of HABP/VABP due to MRSA
  - Moving Target: Continuing evolution of drug resistance
- For individual patients
  - When vancomycin is not an appropriate choice
  - Treatment failures and recurrence
  - Co-morbidities and antibiotic risks vs. benefits
- Telavancin is an important drug for the treatment of HABP/VABP and cSSSI due to *S. aureus,* including MRSA
  - Robust clinical data to support efficacy and safety in both indications

# VIBATIV® (telavancin) for injection

## Important Safety Information (U.S.)

**Mortality**
Patients with pre-existing moderate/severe renal impairment (CrCl ≤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 ≤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**
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 taste disturbance, nausea, vomiting, and foamy urine.



***Full Prescribing Information, including Boxed Warning and Medication Gide in the U.S., is available at www.VIBATIV.com.***

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Medicines That Make a Difference®

# Q&A Session #1

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# Break

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# TD-4208:
# Nebulized LAMA for COPD

**Brett Haumann, MD, MBA**

*Senior Vice President, Development and Operations*

## TD-4208 aims to **address the unmet need** for a standard of care nebulized LAMA

### Potential to be first once-daily nebulized bronchodilator

### Unmet Need:

- Once-daily LAMAs are **first-line therapy** for moderate to severe COPD[1]
- **43%** of COPD treatment regimens in U.S. include a LAMA[2]
- LAMAs are **only available in handheld** devices

### Compelling Market Opportunity:

- **9%** of COPD patients in the U.S. use nebulized maintenance therapy[3]
- Patients suitable for nebulizers are **readily identified** by physicians
- Twice-daily nebulized LABAs generate annual sales of **~$400M**[4]

### First-in-Class Opportunity:

- **No once-daily marketed** nebulized bronchodilators
- **No once-daily** nebulized bronchodilators **in development**
- The only twice-daily LAMA in development is **restricted to one nebulizer**

[1]Global Strategy for Diagnosis, Management, and Prevention of COPD
[2]Encuity Research, LLC., *TreatmentAnswers*™ (2013)
[3]TBPH market research (N = 160 physicians)
[4]Estimate derived from use of information under license from the following IMS Health information service: NSP for period MAT Sep, 2014. IMS expressly reserves all rights, including rights of copying, distribution and republication



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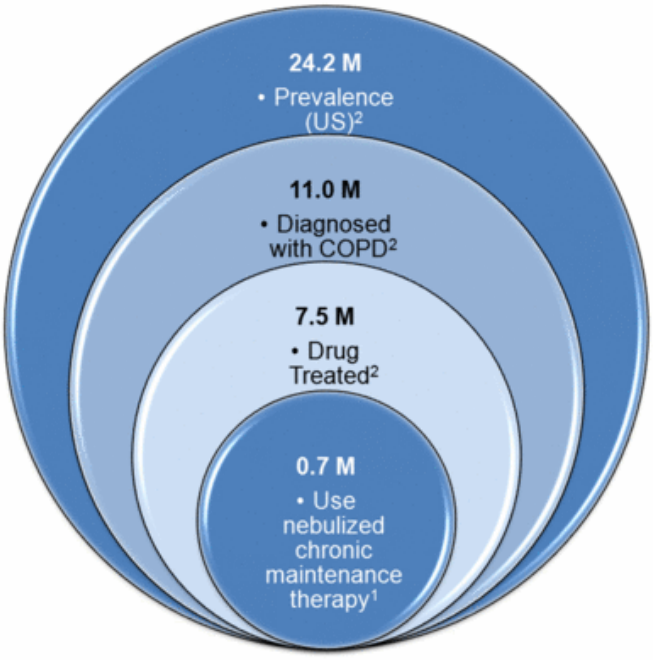
# Despite limited options, **9%** of treated COPD patients in the U.S. use nebulized therapy **on an enduring basis**[1]

## This is in the absence of any nebulized LAMAs




[1]TBPH market research (N = 160 physicians)

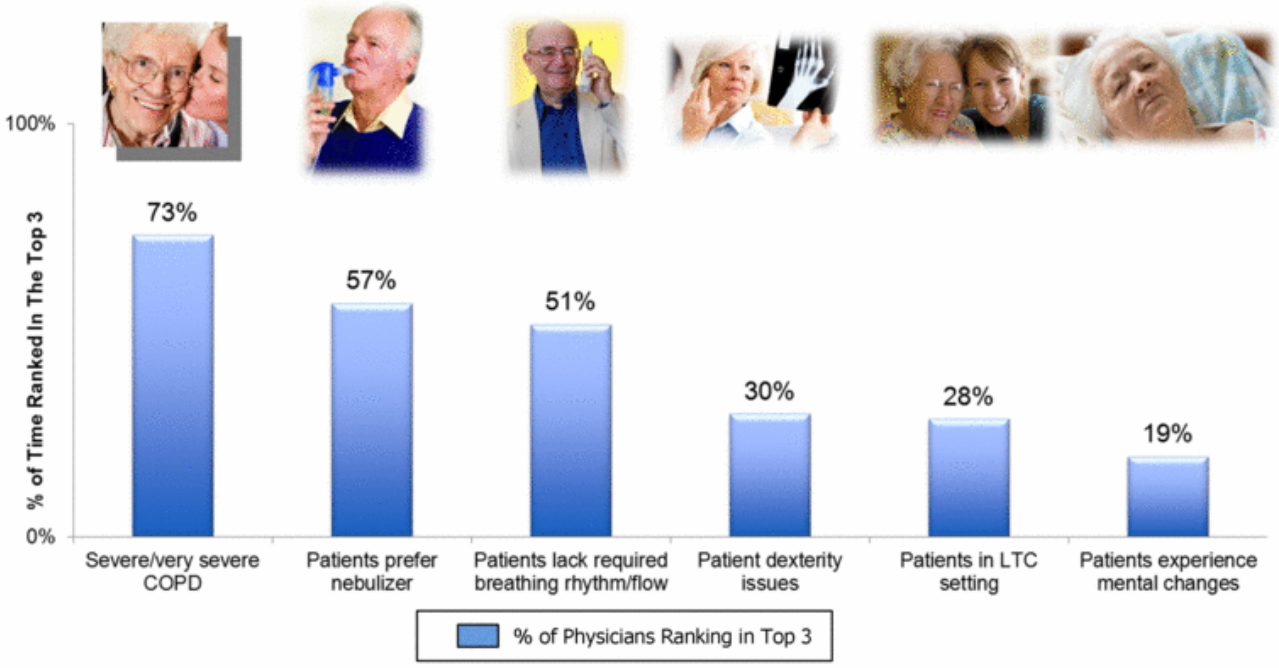




Theravance Biopharma

# Physicians **readily identify** those patients who are most appropriate for nebulizer therapy

## Based on disease severity, patient preference & functional status




[1]TBPH market research (N = 160 physicians)



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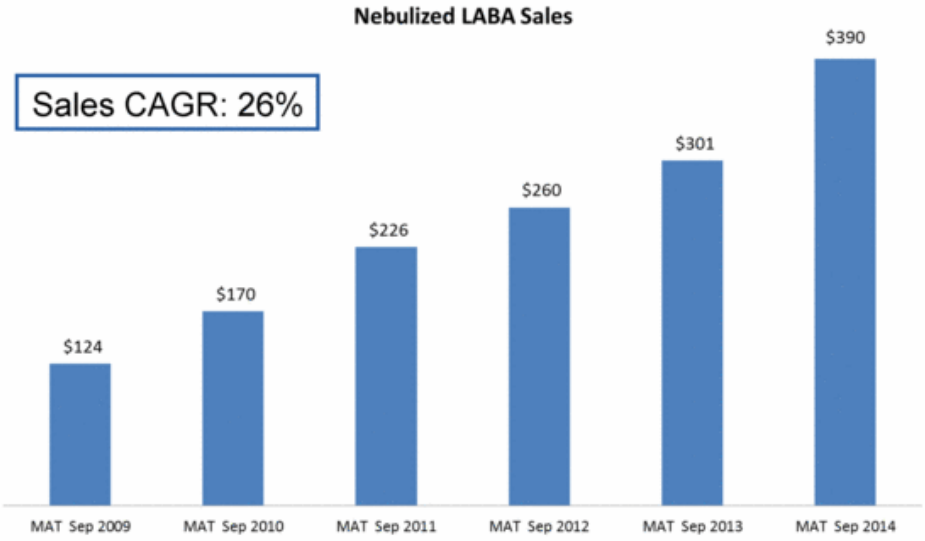
# There are **limited options** for COPD patients who use nebulized bronchodilators

## No nebulized LAMAs and no once-daily products of any class

| Frequency | Class | Handheld segment | Nebulized segment |
|---|---|---|---|
| Four times daily | SAMA | ✓ | ✓ |
| | SABA | ✓ | ✓ |
| | SAMA/SABA | ✓ | ✓ |
| Twice daily | LAMA | ✓ | |
| | LABA | ✓ | ✓ |
| Once daily | LAMA | ✓ | |
| | LABA | ✓ | |
| | LAMA/LABA | ✓ | |

# The nebulized twice-daily LABA market has sales approaching **$400M annually** in U.S.[1]




↗ Growth seen despite generic short-acting bronchodilators, restricted tier status and not being the gold standard LAMA

[1]Estimate derived from the use of information under license from the following IMS Health information service: NSP for the period MAT Sep 2014. IMS expressly reserves all rights, including rights of copying, distribution and republication



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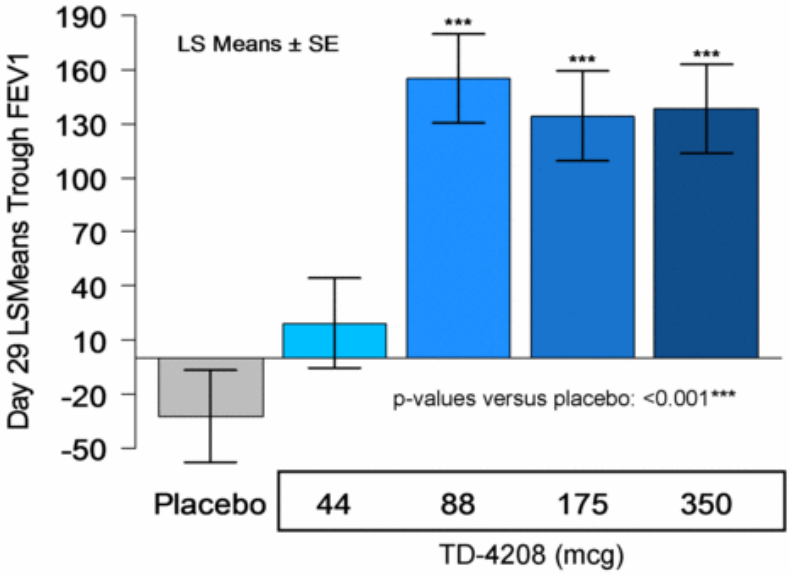
# TD-4208 demonstrates **clinically meaningful improvements** in lung function in COPD patients

## Study 0117 met primary endpoint at doses of 88 mcg and above




- 355 patients with moderate to severe COPD
- Primary endpoint: Change from baseline in trough $FEV_1$ following 28 days

Note: $FEV_1$ = forced expiratory volume in one second. PE = Primary Endpoint. COPD = Chronic Obstructive Pulmonary Disease



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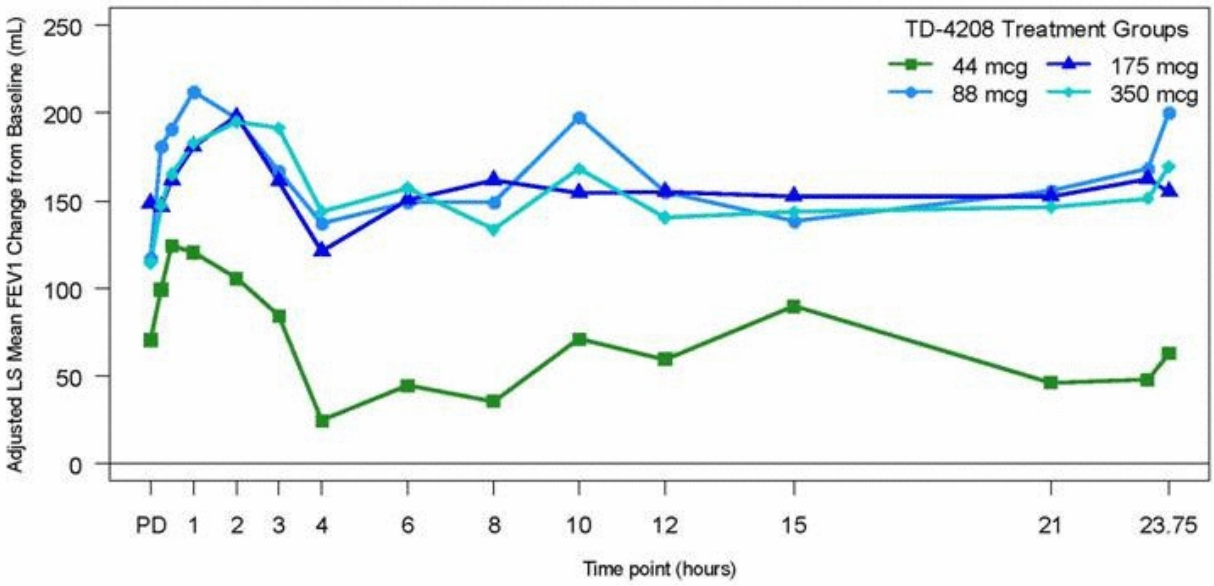
# TD-4208 shows a **sustained 24-hour duration of action** following once-daily dosing

## Effects are maintained throughout 4-week dosing period




Placebo-adjusted change from baseline in $FEV_1$ on Day 28

# The regulatory path is **clear and well-precedented**

## FDA has confirmed that TD-4208 can progress to Phase 3 studies

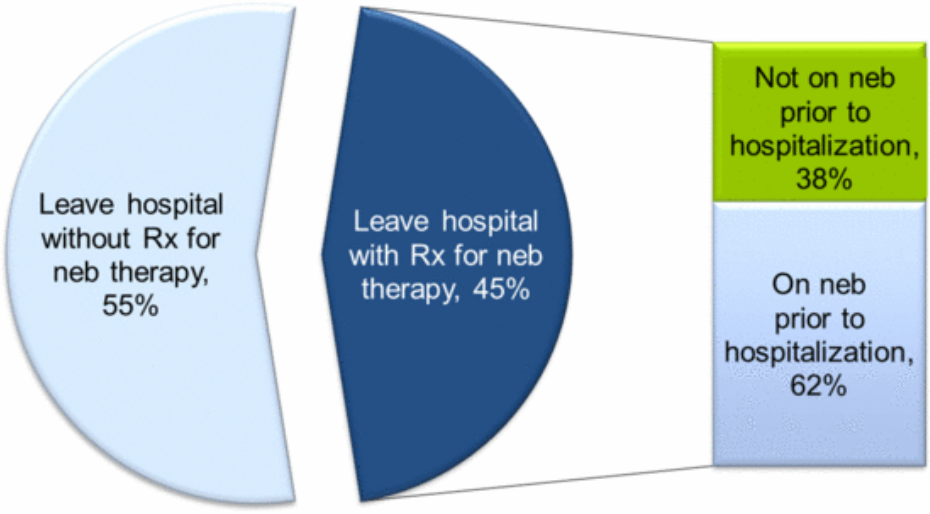
- Phase 3 program **matches** previous LAMA programs:
  - 2 replicate 3-month efficacy studies
  - Single 12-month safety study


- FDA meeting held December 8th
  - ✓ Agreement on once-daily dosing
  - ✓ Agreement on Phase 3 dose selection
  - ✓ Agreement on study population
  - ✓ Agreement on study endpoints

# Nebulized therapy may be initiated in patients **hospitalized with an acute COPD exacerbation**

## COPD is responsible for 800,000 U.S. hospitalizations annually[1]

**Patients Hospitalized for COPD Exacerbations[2]**






[1]Wier et al; HCUP Statistical Brief #106; Agency for Health Care Policy and Research, 2011
[2]TBPH market research (N = 160 physicians)

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# TD-4208 has the potential to become the nebulized **bronchodilator of choice** in COPD

- Aims to become the **standard of care** in the nebulized space
- **Complements** existing nebulized LABA treatment options
- Provides **sustained bronchodilation** over 24 hours
- Offers the **convenience of once-daily dosing** via **jet nebulizer**
- Potential differentiation in patients recovering from **acute exacerbations**
- Presents **opportunities for partnership**

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Medicines That Make a Difference®

# Axelopran:
# Oral PAMORA for Opioid-Induced Constipation

**Brett Haumann, MD, MBA**

*Senior Vice President, Development and Operations*

# Axelopran aims to offer a **differentiated product**

- **Treatment class is evolving:**
  - PAMORAs offer **targeted peripheral efficacy** without altering central analgesia
  - Regulatory path to approval has been **clarified**
  - Recent product approvals will help **build the market**

- **Patient need exists:**
  - Over the counter **laxatives are ineffective** in the majority of patients
  - **71%**[1] of OIC patients using common constipation treatments report **failure to achieve relief**

- **Axelopran program centers on differentiation:**
  - Axelopran aims to **restore normal bowel function** and **reduce symptoms**
  - Encouraging early data for **fixed dose combination**

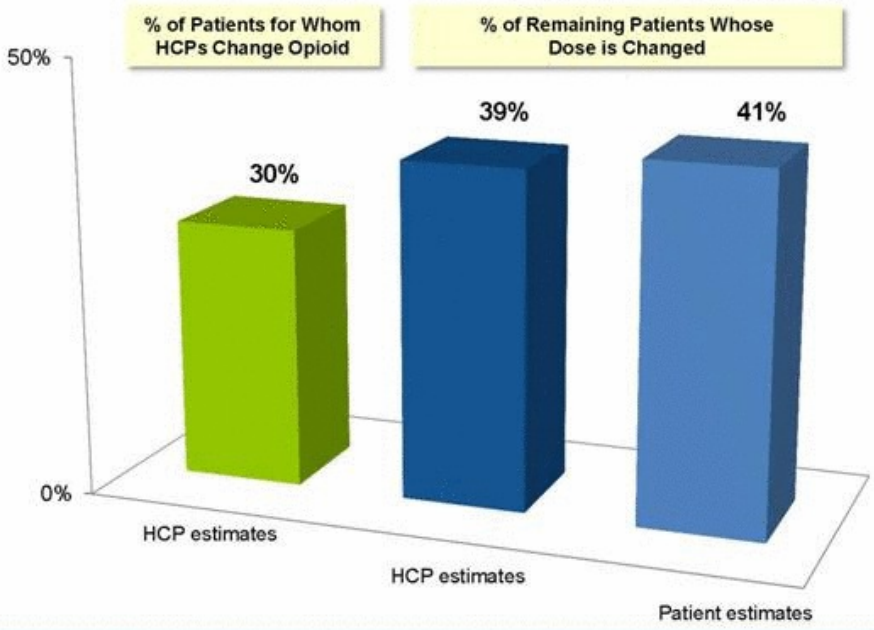

1. Pappagallo et al. American J of Surgery 182 (Suppl) Nov 2001, 11S-18S

# OIC **limits** effective pain management

## OIC results in frequent adjustments to analgesic therapy

**FREQUENCY OF ALTERING PAIN MEDICATION TO MANAGE CONSTIPATION[1]**

- Patients and HCPs -




[1]TBPH patient (N=386) and HCP (N=559) market research



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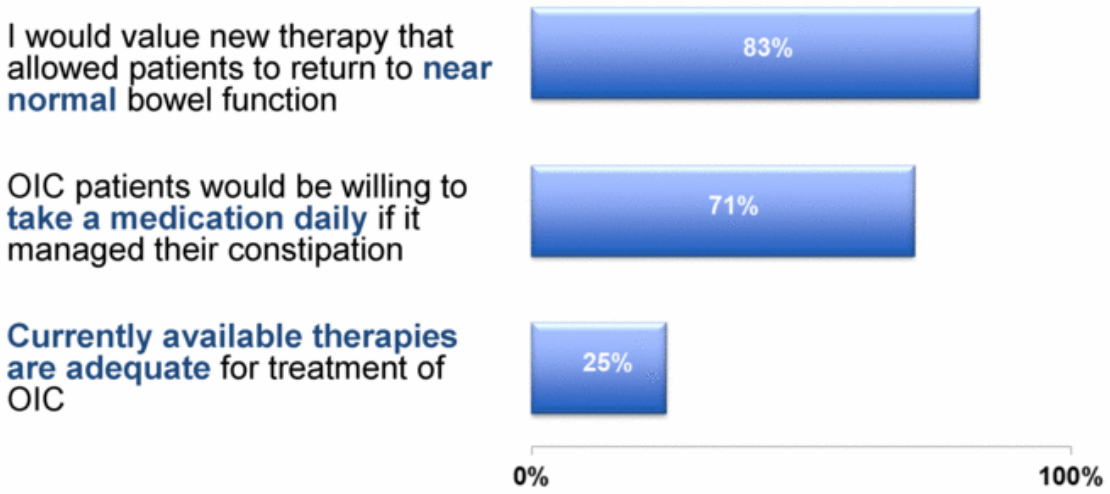
# Health care professionals are **not satisfied** with current treatment options

**HCP ATTITUDES REGARDING OIC TREATMENTS[1]**
- % Top 3 Box -




Agreement rated on a scale from 1 to 10 where 1 means "Disagree Completely" and 10 means "Agree Completely":

[1]TBPH HCP (N=559) market research



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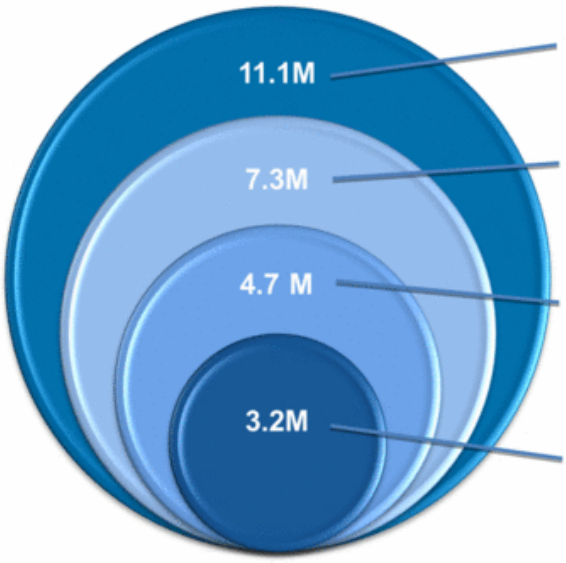
# There is a **sizable, symptomatic and dissatisfied** patient population in the U.S.[1]




**U.S. patients using chronic opioids**
(≥1 episode of ≥90 days per year)

**Patients reporting constipation due to opioids**

**Candidates for axelopran therapy**
(Used OTC laxatives, have discussed OIC with physician, and have drug coverage)

**Strong patient interest in trying a new prescription product to treat OIC**
(≥ 8 on 1 to 10 scale on general interest)

[1]Integrated from longitudinal opioid market assessment performed for TBPH and TBPH patient market research (N=386)



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## The population of OIC patients is **readily accessible** and **not satisfied** with current treatment options

- OIC patients are already in the healthcare system and visit physicians who prescribe their scheduled opioids **every month**
- Patients report discussing OIC with HCPs an average of **4.4 times per year**[1]
- Patients report substantial out of pocket costs for OIC therapies:
  - Spend an average of **$28 per month** for constipation remedies in many cases **without achieving relief**[1]



[1]TBPH patient (N=386) market research

# Theravance Biopharma is **well placed** to access suitable patients within a changing prescribing environment

- Legislative changes are driving a shift in opioid prescribing from primary care to **pain specialists** to reduce overdose-related deaths
- Requirements for **pain clinics to be registered** and physician dispensing prohibited in some states
- **Good fit** with TBPH strategy of **acute care and specialty partnering**

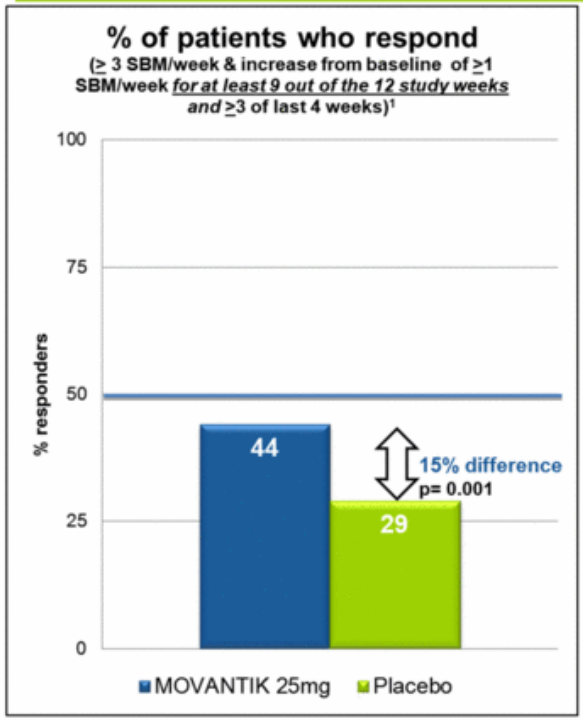

CDC Mortality and Morbidity Weekly Report July 1st 2014: http://www.cdc.gov/mmwr/pdf/wk/mm63e0701a2.pdf

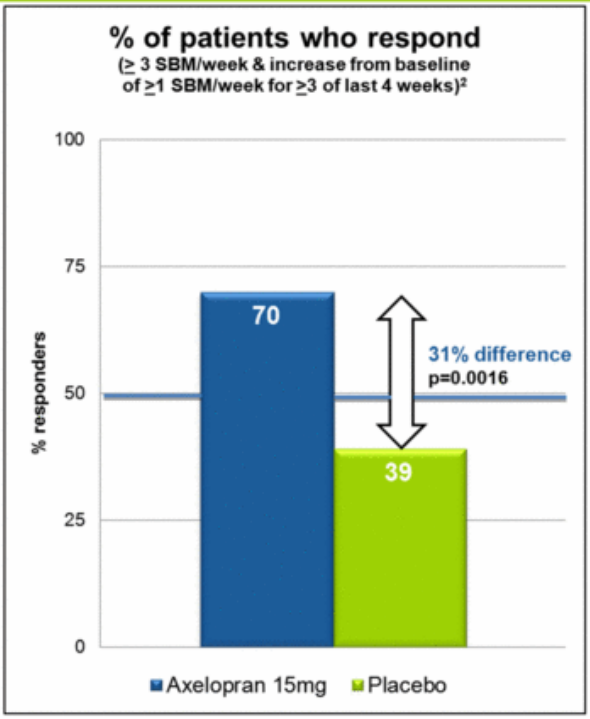
# The axelopran development program is focused on **differentiation**

- Axelopran aims to:
  - Improve bowel function **better than the competition**
  - Restore **normal bowel function**
  - Address **patient symptoms**

# Axelopran Phase 2 data shows **potential for differentiation**

## Improvements in Spontaneous Bowel Movements (SBM) are the current benchmark




1. KODIAK-04 Study
2. Phase 3 axelopran study will include an evaluation comparable to that done for MOVANTIK in Phase 3, including an increase of ≥1 SBM/week for at least 9 out of 12 weeks and >3 of the last 4 weeks of treatment



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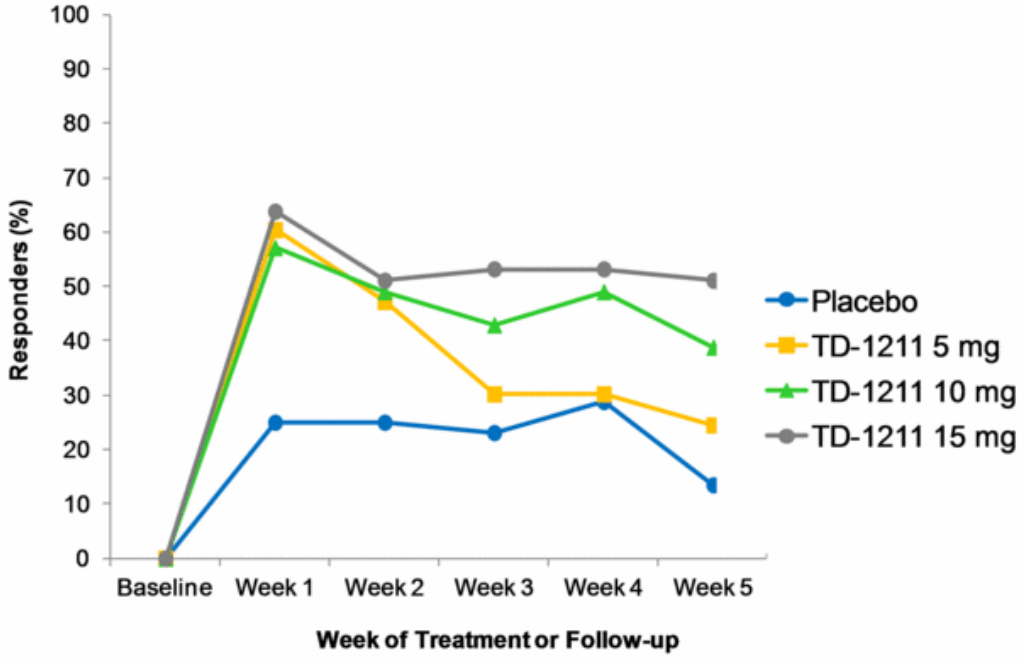
# Rapid restoration of normal bowel function followed by maintenance

## Patients consider ≥**5** SBM/week a return toward normal bowel function




Study 0084



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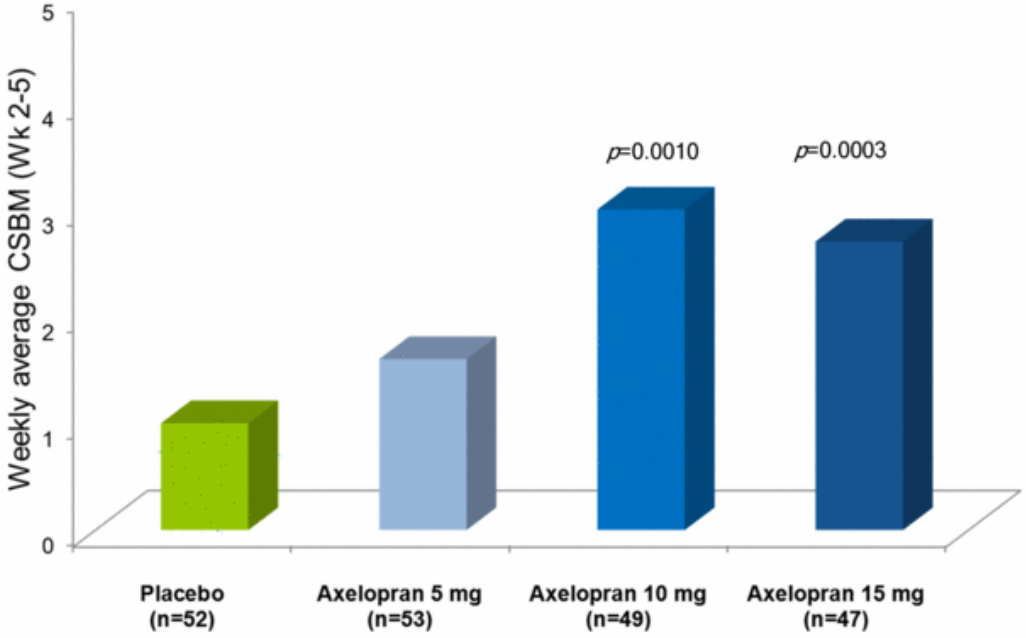
# Increased frequency of Complete Spontaneous Bowel Movements (CSBM)

## Provides a more rigorous assessment of return to normal function



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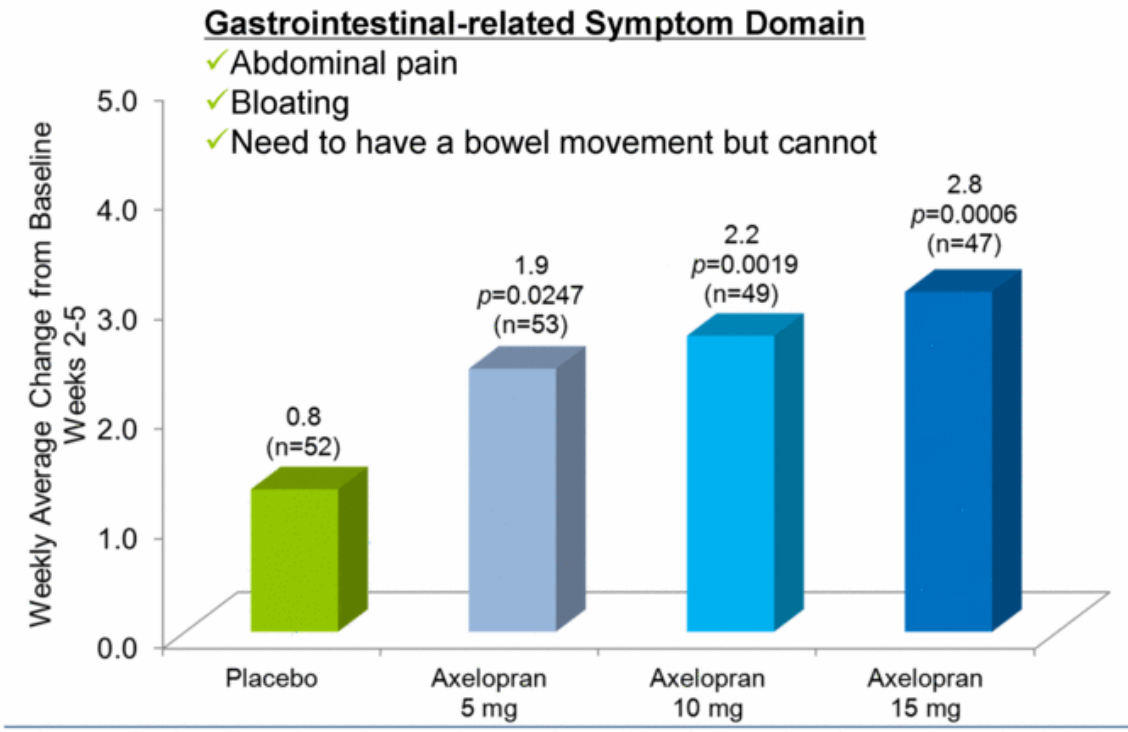
# Improvement in gastrointestinal symptoms

## Suggests potential for differentiation on patient-reported symptoms



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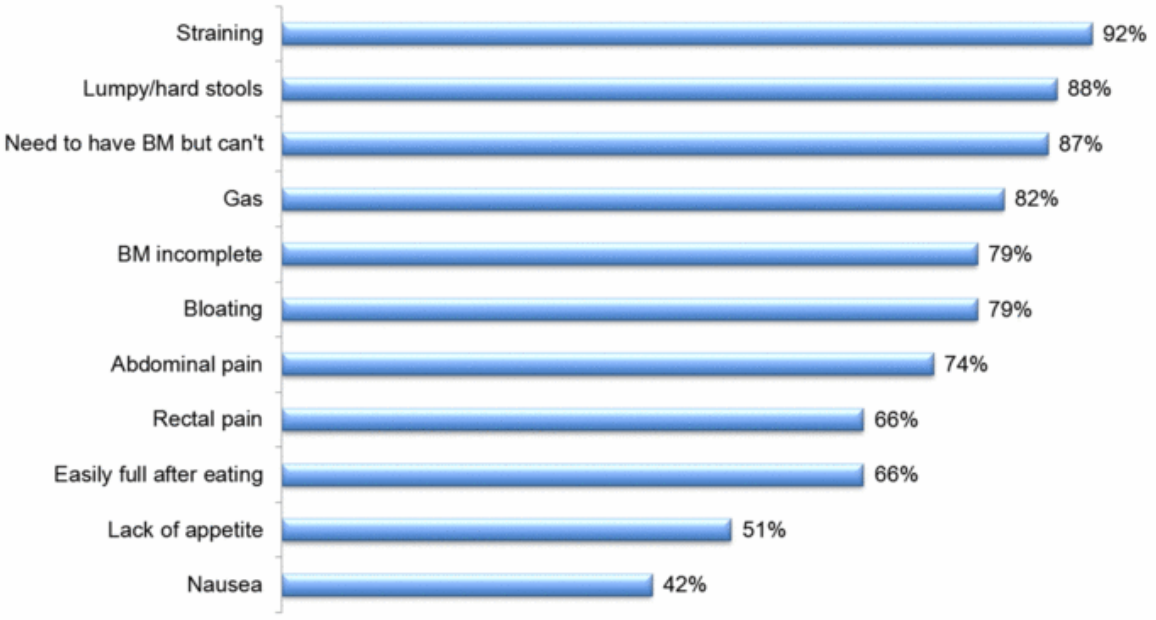
# Patients **need symptom relief** beyond normalizing bowel function

## Increasing SBM alone does not address patients' needs

**Incidence of Constipation Related Symptoms Among OIC Patients[1]**




[1]TBPH patient (N=386) market research



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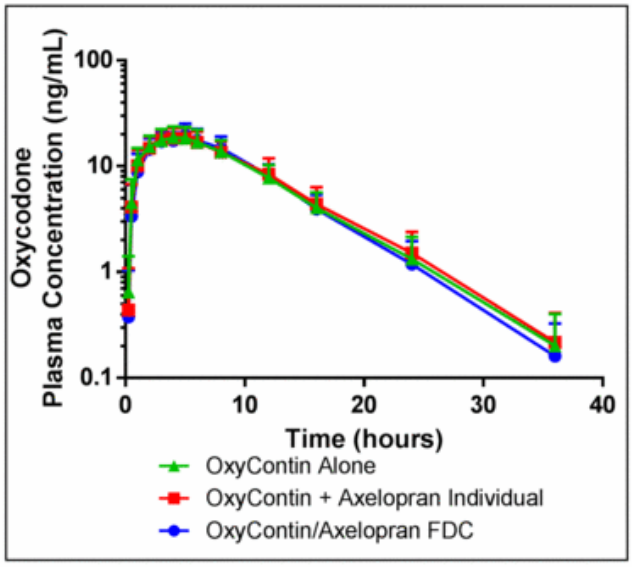
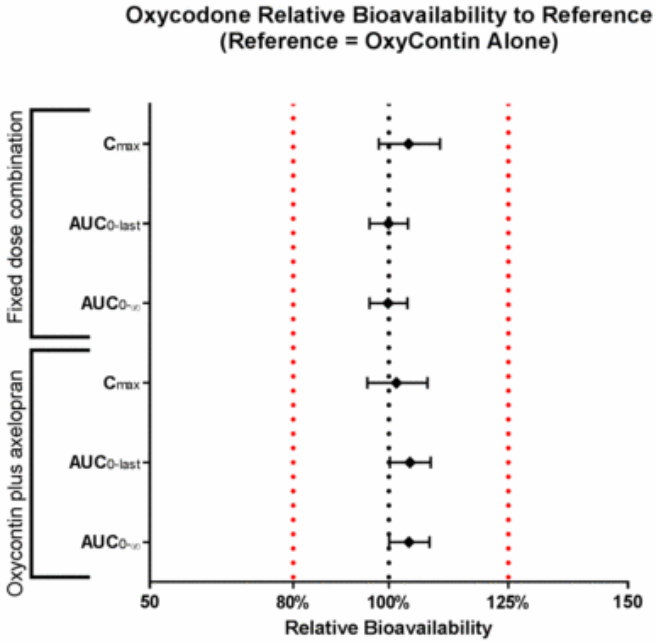
## **Substantial commercial potential** for opioid/axelopran fixed dose combinations (FDC)

- FDC offers the opportunity for pain relief without constipation in a **single abuse-deterrant pill**
  - Could represent a **paradigm shift** in opioid treatment
- TBPH has developed a **proprietary spray-coating formulation**
  - Enabled by the **intrinsic properties** of axelopran
  - Technique could be applied to a broad range of abuse resistant opiates
- **First study** of spray-coat application of axelopran to OxyContin®
  - Designed to evaluate effect of axelopran on **oxycodone exposure**

# Axelopran **does not alter** systemic exposure to oxycodone when delivered as a fixed dose combination (**spray-coating**)



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# Axelopran aims to be the **treatment of choice** for OIC

- **Targeted approach** to address OIC effectively, in contrast to laxatives
- **Large, well-defined, accessible** patient population
- Increasingly managed by pain specialists, aligned with TBPH **focus on specialty business**
- **Clear regulatory pathway and FDA alignment** for axelopran development
- Opportunities for **clear differentiation** based on return to normal bowel function
- Opportunity for fixed dose combination to offer **significant additional value**

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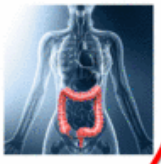
Medicines That Make a Difference®

# Research and Development
## *Evolution of Insight and Approach*

**Mathai Mammen, MD, PhD**

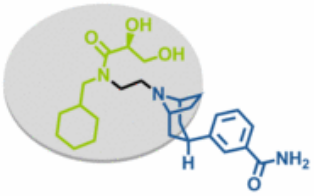
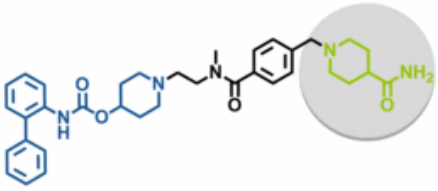
*Senior Vice President, Research and Development*

# Evolution of **Insight** at Theravance Biopharma
## **Multivalent Design** to **Medicines**

| Late Stage | Early Stage | Research |
|---|---|---|
| **Telavancin**<br>Bacteremia | **TD-6450**<br>HCV | **Localized Medicine for Localized Disease** |
| **Axelopran**<br>OIC | **ARNI**<br>Heart Failure |  Lung<br>  GI |
| **TD-4208**<br>COPD | | |

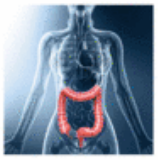
# **Multivalent Design** at Theravance Biopharma

## Examples of Differentiating Features → **Clinical Benefit**

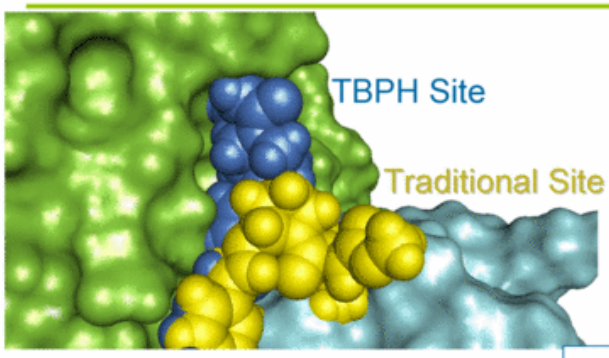
| **VIBATIV®** | **Axelopran (TD-1211)** | **TD-4208** |
|---|---|---|
| Gram-positive antibacterial<br>cSSSI & HABP/VABP | μ-opioid antagonist<br>Opioid Induced Constipation | Inhaled LAMA<br>COPD |
| VIBATIV® (telavancin) for injection |  |  |
| **Dual Pharmacology** | **Controlled Distribution** | **Receptor and Tissue Kinetics** |
| ↓ | ↓ | ↓ |
| Cidality | Peripheral Restriction | Long Acting |

# Evolution of **Insight** at Theravance Biopharma

## **High Potential** Early Stage Programs

| Late Stage | Early Stage | Research |
|---|---|---|
| **Telavancin**<br>Bacteremia | **TD-6450**<br>HCV | **Localized Medicine for Localized Disease** |
| **Axelopran**<br>OIC | **ARNI**<br>Heart Failure |  Lung<br>  GI |
| **TD-4208**<br>COPD | | |

# TD-6450: Multivalent NS5a Inhibitor:
## **Greatest Reported** GT-1a Viral Load Decline after Three Doses




Non-symmetric structure permits **distinct binding mode**

↓

TD-6450 is **highly potent** in vitro against resistance-associated variants across multiple genotypes

NS5a Inhibitors at Progressing Clinical Doses

| Phase 1b: Genotype 1a Patients | TD-6450 | MK-8742 | GS-5816 | ACH-3102 | IDX-719 |
|---|---|---|---|---|---|
| Mean Reduction HCV GT-1a RNA ($log_{10}$ IU/mL) | **-5.00** | -4.17 | -3.56 | -3.78 | -3.50 |

***8/21 Patients at doses >120mg had viral loads <LOD***

Go Alone (U.S. - Acute) | **Partner** | **Monetize/Divest**



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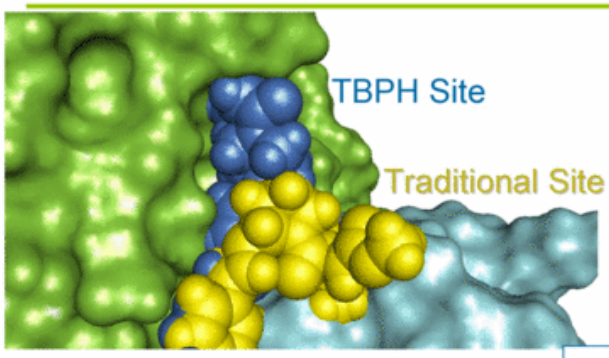
# TD-6450: Multivalent NS5a Inhibitor:
## **Greatest Reported** GT-1a Viral Load Decline after Three Doses

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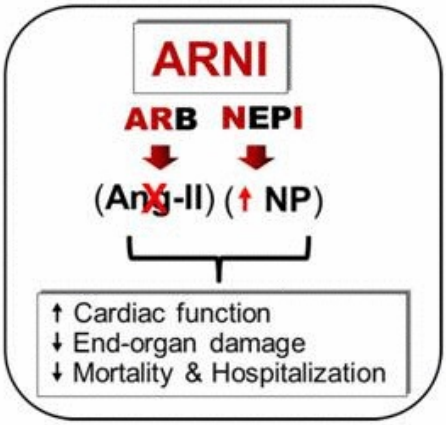
***On November 24th 2014 TD-6450 granted Fast Track Designation by FDA***

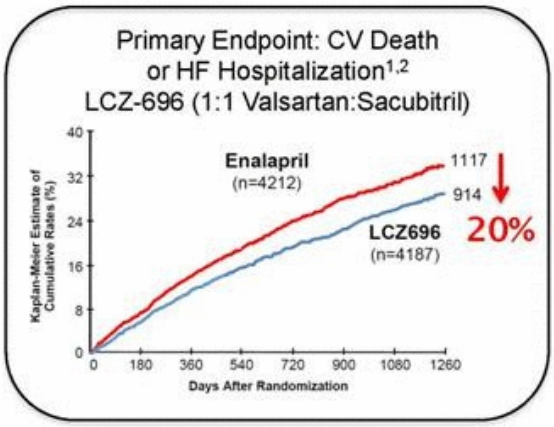
Go Alone (U.S. - Acute) | **Partner** | **Monetize/Divest**



Theravance Biopharma

# ARNI Class of Medicines May be a Paradigm Shift for Patients with Congestive Heart Failure




**However, important considerations:**

- **Inflexible 1:1** valsartan:sacubitril
- **Excluded patients** with severe renal dysfunction (~ 1M patients)[3]
- **Symptomatic Hypotension**



[1]McMurray et al (2014) *N Engl J Med*, 371:993-1004
[2]Solomon et al (2012) *Lancet*, 380:1387-95

[3]TSPH estimate based on integrating data from multiple sources

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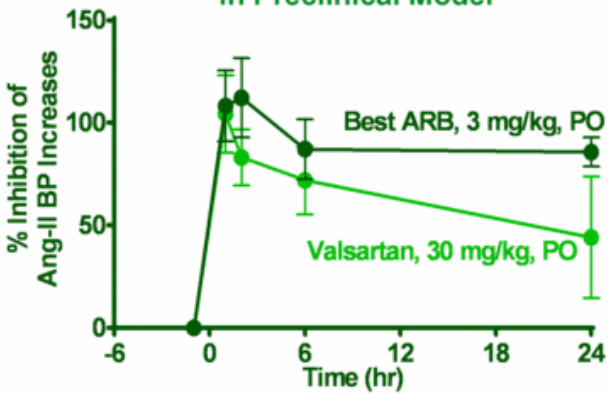
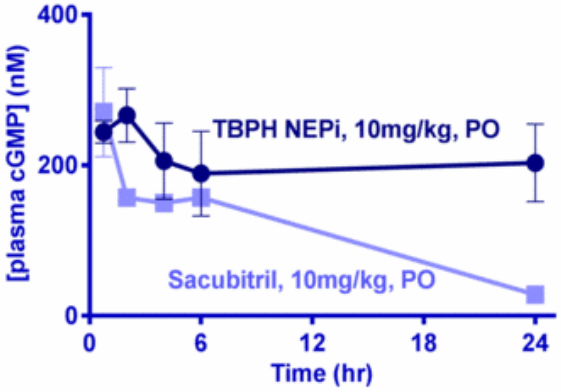
# Our **Objective** is to Create a **Best-in-Class** ARNI for Heart Failure

Best ARB + Best NEPi = **Best ARNI**
Improved efficacy
All HF patients
QD dosing

**Sustained Ang II Receptor Blockade in Preclinical Model**




**Sustained Neprilysin Inhibition in Preclinical Model**




Value Inflection in Phase 1b / 2a



Theravance Biopharma

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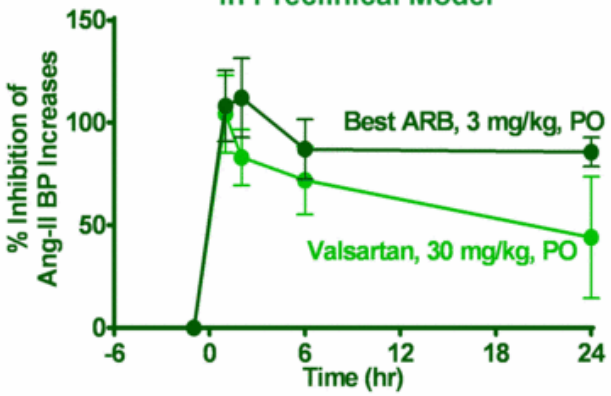


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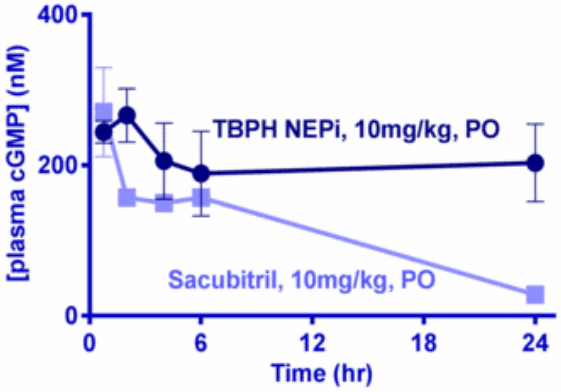


Go Alone (U.S. - Acute) | Partner | Monetize/Divest



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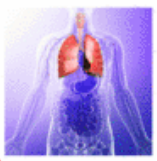
# Evolution of **Insight** at Theravance Biopharma

## **15+ Years of Learning** Led to Research Strategy

| Late Stage | Early Stage | Research |
|---|---|---|
| **Telavancin**<br>Bacteremia | **TD-6450**<br>HCV | **Localized Medicine for Localized Disease** |
| **Axelopran**<br>OIC | **ARNI**<br>Heart Failure | |
| **TD-4208**<br>COPD | | |



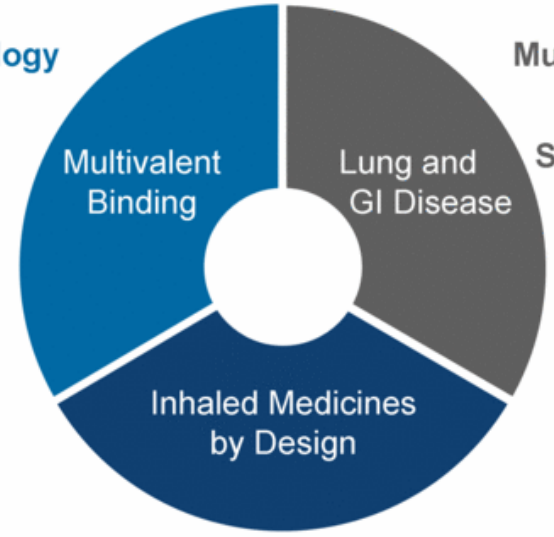
Lung

GI

***Goal of localization is enhanced efficacy in target tissues and limited systemic side-effects***

# Biological and Chemical **Research Insights** Evolved Over 15 Years Along Three Dimensions

**Dual Pharmacology**
**Selectivity**
**Kinetics**




**Multiple Successful P2 Studies**
**Expertise in:**
**Smooth Muscle Biology and Immuno-Inflammation**
**Disease Insights**

**"Design-in" Tissue Kinetics,**
**Dynamics and Systemic Clearance**
**Translatable to GI Lumen-Restricted Drugs**



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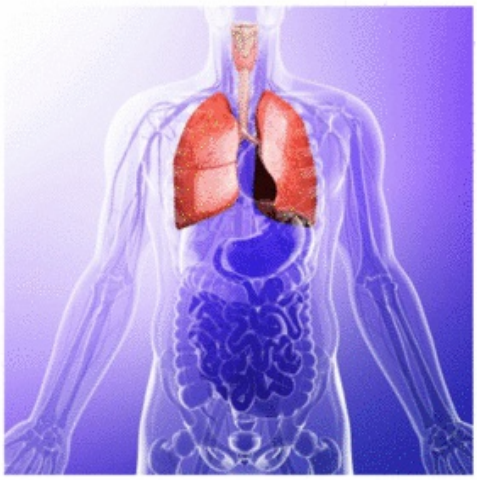
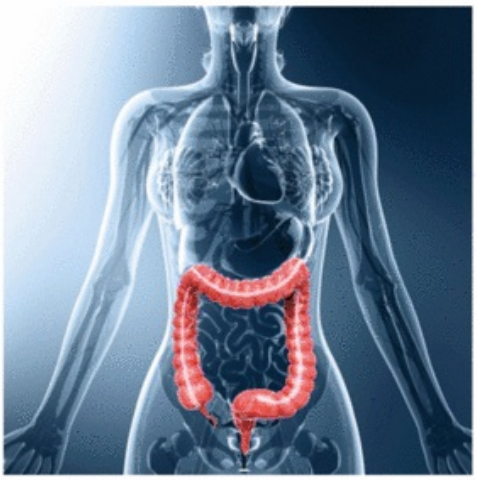
# Localized Medicines for Localized Diseases

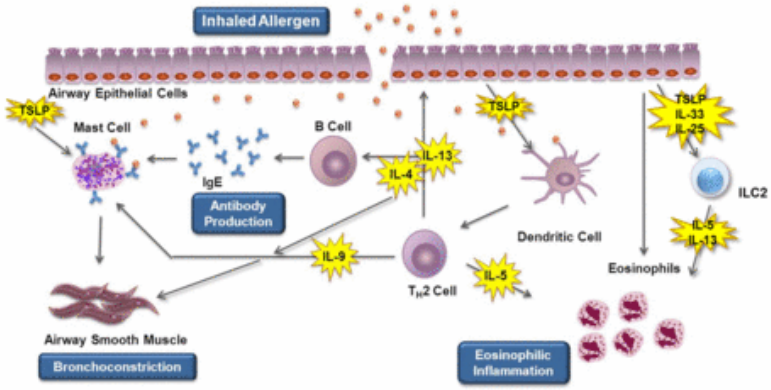
## Leveraging Multivalent Design to Treat Severe Immuno-inflammatory Diseases of Lung and GI Tract





# Control is **Significant Challenge** for Severe Asthma

- ~ 2M asthmatics (U.S. + EU) refractory to high-dose bronchodilator/ICS therapy[1]
  - 10-15% patients account for ~50% of asthma budget[2]
  - Small subgroups benefit from Biologics




***Asthma is a complex, heterogeneous disease and inhibition of multiple mediators may be required for optimal efficacy***

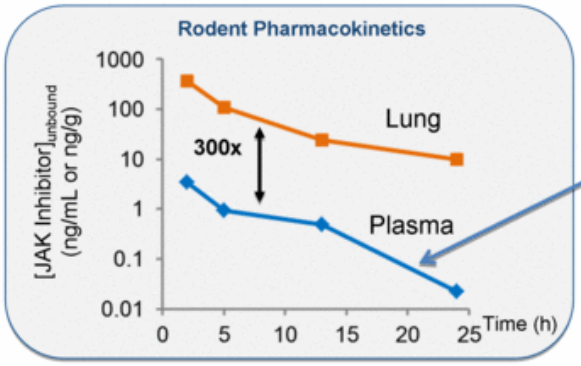


[1]TBPH estimate based on integrating data from multiple sources
[2]Gaga et al (2009) *Eur Respir Rev*, 18: 112, 58-65

# We are Creating **Broadly Active** Inhaled Inhibitors of JAK as **Powerful** Potential Treatment for **Severe Asthma**

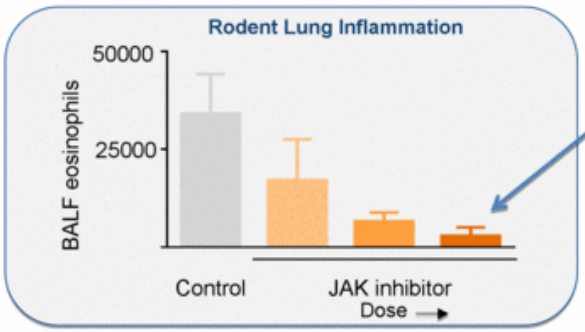
JAK is indirectly **clinically validated** by anti-cytokine biologics

*Localized Drug*




*Low risk*

*Targeted Benefit*




*High Impact*

**Potential applications beyond severe asthma**



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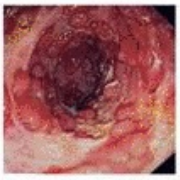
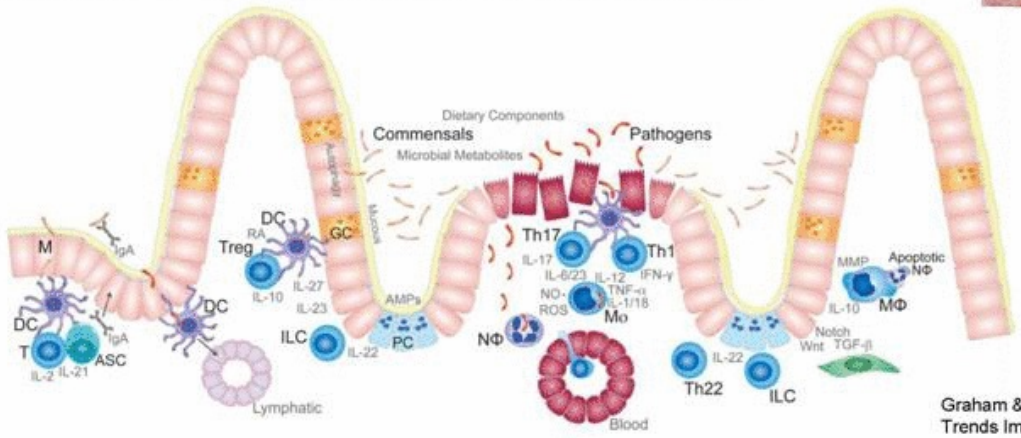
# **Ulcerative Colitis**: A Major **Unmet Medical Need** Remains

- ~ 680K patients in the U.S.[1]
- Current treatments have limited efficacy, lose efficacy with time, or are inappropriate for long term use






Graham & Xavier (2013)
Trends Immunol., 34: 371-378

***UC is a complex, heterogeneous disease, and optimal therapy may require targeting multiple inflammatory pathways***

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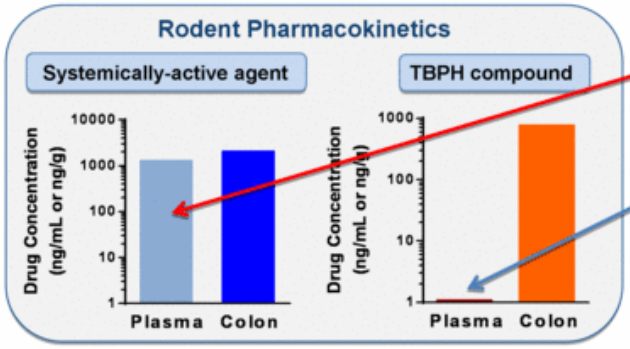
# We are Creating Oral Small Molecules for Ulcerative Colitis that are **Restricted to the GI Tract**

TBPH target addresses multiple inflammatory mediators

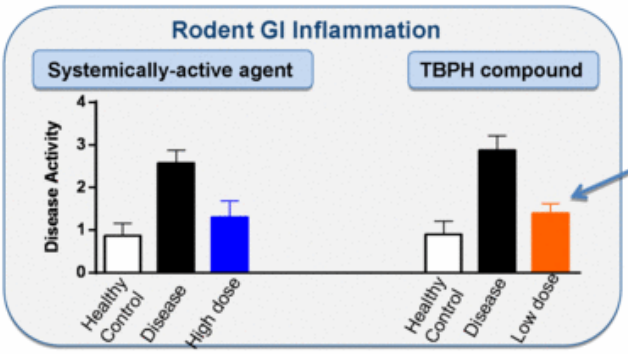
*Localized Drug*




*High risk*

*Low risk*

*Targeted Benefit*




*High Impact*

Potential applications beyond UC



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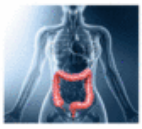
# **Evolution of Insight** at Theravance Biopharma

## High Potential Early and Late Stage Programs

- We make highly impactful medicines based on our experience and our understanding of patient needs
- Today's Research leverages 15+ years of evolution of insight
- Multiple programs poised to deliver value in the near and medium term

| Late Stage | Early Stage | Research |
|---|---|---|
| **Telavancin**<br>Bacteremia | **TD-6450**<br>HCV | **Localized Medicines for Localized Diseases** |
| **Axelopran**<br>OIC | **ARNI**<br>Heart Failure |  **Lung**  **GI** |
| **TD-4208**<br>COPD | | |

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# Financial Highlights and Outlook

**Renee Gala**

*Chief Financial Officer*

# Financial Highlights and Outlook

# Financial Management of Business

## Starts with a Focus on Insight and Innovation


***Objective of Tax Efficient*** *Corporate Structure is to* ***Optimize Future Cashflows***

# Financial Management of Business

## Applying Insight and Innovation to Financial Operations

# VIBATIV® and TD-4208 Drive Investments in 2015

## Investments in Other Programs Depend on Multiple Factors

# Financial Guidance May be Impacted by Partnering and Other Factors

## 2015 Financial Guidance

- *Operating Loss: $150 – 160M †*
  - *Excluding stock-based compensation*
  - *Likely to be front-loaded*
  - *VIBATIV® net sales of approximately $20M*
- *Factors that May Impact Guidance:*
  - *Partnering*
  - *Data and other program-related decisions*

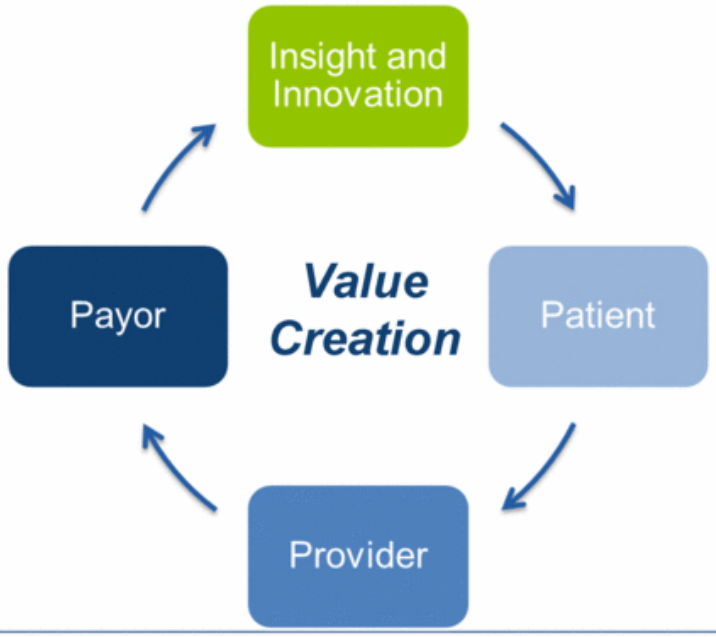


† Non-GAAP Operating Loss, excluding stock-based compensation

# The Theravance Biopharma **Strategy**

## **Insight and Innovation** Important in Everything We Do

***Leverage Our Insights to Make a Difference for Patients and Create Meaningful Value for Shareholders***



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# Q&A Session #2

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# Thank You